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VA HEALTH CARE Defining EXCELLENCE in the 21st Century

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VA HEALTH CARE Defining EXCELLENCE in the 21st Century

ADVANCES IN PAIN MANAGEMENT FOR VETERANS: CURRENT STATUS OF RESEARCH AND FUTURE DIRECTIONS

Robert D. Kerns, PhD; Alicia A. Heapy, PhD

Military Veterans have been identified as being particularly vulnerable to the development and perpetuation of pain [1]. Among the 23 million U.S. military Veterans, it has been estimated that as many as 50 percent of male Veterans and as many as 75 percent of female Veterans experience chronic pain [2]. Painful musculoskeletal conditions are the most common disorders among Veterans returning from the recent conflicts in Iraq and Afghanistan, surpassing the rates of all mental health conditions combined [3]. Pain among these Veterans is highly comorbid with the "signature injuries" of these conflicts, namely posttraumatic stress disorder (PTSD) and traumatic brain injury [4]. Although not unique to Veterans, compounding the challenges associated with successful management of chronic pain is continued evidence of a provider workforce that is ill-prepared to assess and manage common pain conditions [5], limited effectiveness of analgesic medications and other nonpharmacological approaches [6], and growing concerns about harms associated with long-term opioid therapy [7]. In 2011, the Institute of Medicine (IOM) published its seminal report, "Relieving pain in America: A blueprint for transforming prevention, care, education, and research," and called on the Department of Veterans Affairs (VA) and other Government and stakeholder groups to renew their commitment to this national transformational effort [1].

This special topic issue of *JRRD* presents results from pain research projects taking place in the VA healthcare system, with a focus on innovative research and its practice and policy implications.

Research on pain among Veterans is not new. In fact, some of the early pioneering work to advance the multidimensional assessment of chronic pain and establish the efficacy of psychological approaches for pain management was conducted in the VA [8–9]. By 1998, former VA Undersecretary for Health Kenneth Kizer, MD, identified the need for more pain research as one of the objectives of a VA Pain Management Strategy [10]. A special topic issue of the *Journal of Rehabilitation Research and Development* (*JRRD*) in 2007 highlighted sustained growth in the VA pain research portfolio [11], and annual reports since that time provide evidence of yearly growth in terms of the number, scope, and financial expenditures in support of the VA's pain research portfolio.

This special topic issue of *JRRD* presents results from pain research projects taking place in the VA healthcare system, with a focus on innovative research and its practice and policy implications. The specific objectives of the issue are to educate readers about (1) special issues faced by Veterans with pain, especially Veterans of the recent wars in Iraq and Afghanistan; (2) potential sources of inequities in pain care that may have special relevance for Veterans; and (3) novel approaches to the assessment and treatment of pain and comorbid conditions for Veterans with pain. As such, contributions to this special issue come from the VA clinical, rehabilitation, and health services research communities as opposed to investigators conducting basic laboratory science and preclinical research. Ultimately, we hope that the series of original articles that comprise this special issue will convey a sense of the robust pain-relevant research program in the VA and inform an agenda for further research addressing the management of pain in Veterans and other groups.

Contributions to this special topic issue offer a window into the exciting, innovative, and important pain-relevant research being conducted in the VA that directly informs the VA's efforts to address the challenge of the IOM. As just one example, a key finding of the IOM was the lack of consistent data that document the incidence and prevalence of pain and its effects on activities

of daily living and work, use of healthcare and social services, and costs of pain and pain care and the recommendation to "improve the collection and reporting of data on pain" [1]. The VA is ideally positioned to address this recommendation because it has one of the most comprehensive electronic health record (EHR) systems in the United States, which includes longitudinal clinical assessments (e.g., pain intensity screening), treatments, and outcomes data. These clinical data are complemented by a comprehensive registry of administrative and descriptive data for Veterans in VA care. Given this important strength of research conducted using VA data, it is gratifying that a number of articles in this special topic issue report on analyses of VA administrative and clinical data to address gaps in the epidemiology of pain and pain care and inform quality and performance improvement initiatives and additional research.

The special issue begins with a contribution by Erica A. Abel, PhD, et al. that shares results of a survey of VA clinical and health services investigators regarding the perceived use of VA data for observational research and opens the discussion on the use of these data to define key constructs such as "chronic pain" and "long-term opioid therapy." This foundational article is followed by several that used observational methods to examine key questions using VA's electronic data. One of the earliest VA investigators to use VA data to examine pain care in VA is Diana J. Burgess, PhD. In this special topic issue, Burgess et al. use the VA's Survey of Healthcare Experiences of Patients (SHEP) data matched with EHR data from the selected sample of Veterans who participated in the SHEP to examine whether pain outcomes (pain interference, perceived pain treatment effectiveness) vary by race and then whether opioid use moderates these associations. Three articles used similar methods to examine pain and important comorbidities. Travis I. Lovejoy, PhD, MPH, et al. examined Veterans with comorbid pain and substance use disorders and predictors of receipt of opioid therapy, usually contraindicated for this population due to the risk of prescription opioid addiction, exacerbation of other substance use disorders, and other harms. Samantha D. Outcalt, PhD, et al. used clinical and administrative data to examine whether pain moderates receipt of guideline-concordant treatment for Veterans with PTSD. Unfortunately, Veterans who had a positive screen for PTSD and documented chronic pain were less likely to receive mental health care relative to those without comorbid chronic pain. April F. Mohanty, MPH, PhD, et al. from the War Related Illness and Injury Study Center (WRIISC), which emphasizes research on Veterans from recent conflicts in the Middle East, used longitudinal VA data to examine comorbidities and the course of care for Veterans with fibromyalgia syndrome. The methods employed in these studies can serve as important models for future research using VA's EHR system and other databases to address the IOM's charge for high-quality epidemiological research that examines pain and pain care.

This series of studies is complemented by two articles that employed survey methods to examine pain and important comorbidities. Lisa M. McAndrew, PhD, also from WRIISC, and her colleagues report on findings that significantly extend our understanding of pain in the context of a larger condition of diffuse chronic multisymptom illness (CMI). They used data from a longitudinal study of Veterans from the recent wars in Iraq and Afghanistan to document that a majority of Veterans from this era reported the presence of symptoms consistent with CMI and that approximately 90 percent of Veterans reporting pain met the criteria for CMI. Further, CMI was associated with significantly worse physical health functioning that was not accounted for by concurrent PTSD. Diana M. Higgins, PhD, et al. examined data from the MOVE!23 survey that is routinely collected from Veterans participating in MOVE!, VA's weight-management program. Among those completing the survey, 72 percent reported painful conditions. Particularly provocative was the observation that pain was associated with multiple other medical and mental health comorbidities. Together, these studies all argue for consideration of pain as a surrogate or marker for poor health, generally speaking, and strongly reinforce emerging observations that pain may be an important moderator and/or mediator of other health conditions and their treatment and outcomes of treatment.

Shifting from studies using observational data, three articles report on secondary analyses of data collected in the context of treatment for chronic pain. In the first of these reports, Jennifer L. Murphy, PhD, et al. from the VA's award-winning Chronic Pain Rehabilitation Program at the James A. Haley Veterans' Hospital examined the influence of sex as a moderator of treatment outcome and maintenance of its effects. Most striking was the observation that female Veterans were less likely than male Veterans to maintain improvements in pain intensity and sleep quality at a 3 mo follow-up evaluation following completion of the 3 wk residential program. Treatments that promote healthy

lifestyles, including exercise, walking, and structured activity, have begun to be documented as important strategies for reducing pain and improving functioning among those with chronic pain. In a highly innovative and exciting line of research, Erica Scioli-Salter, PhD, et al. reported on pilot data from a randomized trial of cardiopulmonary fitness for trauma-exposed Veterans who were otherwise healthy or had chronic pain and comorbid PTSD. In this context, the investigators demonstrated neurobiological correlates of pain threshold and tolerance during an analog task 30 min after exercise, providing preliminary evidence of a neurobiological mechanism for the hypothesized analgesic effects of exercise. Sarah L. Krein, PhD, RN, et al. examined the effects of a walking intervention for Veterans with chronic back pain, some of whom were concurrently being treated with long-term opioid therapy. They reported that those receiving long-term opioid therapy were not only willing to participate in the exercise program but that they actually improved their daily steps more than those not receiving opioid therapy, suggesting an incremental benefit of a structured walking program for Veterans receiving long-term opioid therapy. Together, these articles lend support for integrating exercise into a multimodal plan of care for Veterans with chronic pain.

Finally, this issue includes four articles that report on aspects of important VA practice and policy initiatives. Carol Elizabeth Fletcher, PhD, RN, et al. address the VA's efforts to promote core concepts of patient-centered care, especially the increased use of complementary and integrative health approaches. Their data provide confirmatory evidence of the perceived interest of Veterans in both inpatient and outpatient settings in using these approaches. A contribution by William C. Becker, MD, et al. reports on preliminary development of a novel approach to screening for harm, benefit, and misuse of opioid medications in the primary care setting. This work is entirely consistent with the VA's Opioid Safety Initiative designed to promote safe and effective long-term opioid therapy for a select group of Veterans who may benefit from this therapy. Brent A. Moore, PhD, et al. report on results of efforts at one VA facility and a non-VA Federally Qualified Health Center to implement the Stepped Care Model of Pain Management that was described by the IOM as a potential model of integrated, evidence-based, and patient-centered care. Finally, Evan P. Carey, MS, et al. report preliminary findings that document substantial geographic dispersion of VA's Specialty Care Access Network-Extension of Community Healthcare Outcomes (SCAN-ECHO) initiative that uses video conferencing to promote case-based learning to enhance the competencies of primary care providers in their care of Veterans with pain.

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DEPARTMENT OF VETERANS AFFAIRS OFFICE OF RESEARCH AND DEVELOPMENT'S PAIN PORTFOLIO

Audrey N. Kusiak, PhD

It is an exciting time for pain research at the Department of Veterans Affairs (VA). In the seven years that I have been a Scientific Program Manager in the Rehabilitation Research and Development Service in the Office of Research and Development (ORD), I have witnessed an increase in the number of projects and funded investigators within VA's pain portfolio. In 2009, there were approximately 57 projects on pain research. In July 2015, the number of projects was 109, and importantly, the investment in pain research almost tripled within this time span. This change can be attributed to the increased interest in pain research within VA's scientific and clinical communities brought about by the unique chronic pain management needs of Veterans returning from Iraq and Afghanistan and the collaborative effort between VA's pain research community and ORD to spotlight pain research. Pain research in ORD appropriately spans the translational research spectrum and includes basic/foundational research mainly in animal models, epidemiology to determine the distribution of various painful conditions in the VA, pain diagnosis, management and treatment of pain, underlying causes of chronic pain including the transition from the acute to chronic state, adverse events associated with pain management, and health services-level research. This editorial covers a fraction of the innovative and unique areas of pain research being conducted at the VA and the important role VA researchers play in the pain community, as evidenced by VA participation in the Interagency Pain Research Coordinating Committee (IPRCC) National Pain Strategy (NPS).

VA's research programs are unique entities, serving as platforms and resources for the research community and the Veterans we serve.

- Pain management: The challenge of treating Veterans with chronic pain and coexisting conditions has sparked an interest in how to care for these individuals effectively. Team-based integrative approaches play up to VA's strengths as a healthcare system and include the clinicians who see Veterans in the clinic, who also conduct basic up to health services research. This is reflected in the high number of treatment-related projects (n = 46) examining the effectiveness of exercise and activity; complementary approaches, including electroceuticals (e.g., transcranial magnetic stimulation) and yoga; and testing different formulations of drug therapies focused not only on pain but also on coexisting conditions, including posttraumatic stress disorder (PTSD), depression, sleep, and substance use disorders. The emphasis of treatment includes reduced dependence on opioids as "go to" drugs and examining alternate forms of pain management, putting the Veteran in the driver's seat in managing the painful condition.
- Comparative-effectiveness research: Comparative-effectiveness studies emphasize the importance of "evidence-based practice" and "practice-based evidence" results and are reality checks as to what treatments should be effective and what treatments actually are effective. These types of studies are unique to healthcare systems and aim to improve the delivery of care and maximize patient satisfaction while being cost-effective. It is an area of research well-suited to the VA and an area in which the VA Health Services researchers are leaders in the field. Results from these studies change the way care is delivered at the VA. An example of evidence-based practice research is the adoption of acupuncture for chronic low back pain at the VA, while an example of practice-based evidence research is the ongoing assessment of the Stepped Care Model for pain management. In this case, results recommend the rearrangement of "steps" to make the process more efficient and effective, including rotating the clinicians versus having the patient rotate through the

"steps." Comparative-effectiveness studies are an ideal way to determine best practices that benefit the Veteran.

- Precision medicine: Everyone is talking about precision medicine, but VA pain researchers and clinicians are actually "walking the walk." The Institute of Medicine (IOM) prominently mentioned VA's Stepped Care/Patient Aligned Care Teams (PACTs) as a model for pain management, which includes the patient as a member of the pain management team, thus ensuring individualized treatment, patient participation, and adherence to the treatment plan that they helped develop. Another emerging area of personalized pain management is the screening of individuals with neuropathic pain for mutations in sodium channel dysfunction. Neuropathic pain caused by disease or injury results in alteration in sodium channel function. Genetic mutations in sodium channels result in a gain of function or loss of function with a concomitant change in sensitivity to painful stimuli. This genetic screening approach has been effective in determining who will respond to sodium channel antagonists and the subsequent alleviation of pain in genetic conditions such as erythromelalgia. It is hoped that the technique can be extended to other neuropathic painful conditions, including diabetes and spinal cord injury.
- Pain diagnosis/testing: Pain research occurs in the least likely of places, including the field of regenerative medicine. VA researchers are incorporating pain measurements following the transplantation of ex vivo engineered tissues and cells for joint replacement and spinal cord injury to demonstrate safety and lack of adverse side effects, namely pain. Tissue engineering for musculoskeletal and neurological disorders is a viable alternative if the transplanted tissue does not produce or exacerbate already existing pain. Screening for pain early on in the research and development process decreases the chances that a cell therapy that does not alleviate pain or creates pain will advance to costlier larger animal models or human trials.
- Unique programs: Musculoskeletal pain as a result of Active Duty is often chronic and ranks among the highest in terms of clinic visits. The Musculoskeletal Cohort is a longitudinal project tracking Veterans living with musculoskeletal pain of various etiologies, including osteoarthritis, joint pain, back and neck pain, nerve compression, and other painful conditions originating from a musculoskeletal origin. The Musculoskeletal Cohort is providing VA researchers with data on the occurrence, treatment, and screening of pain; presence of coexisting conditions; and cost of musculoskeletal pain care. Such data can then be analyzed to determine what works and what does not work, and for whom, thus streamlining the process of pain management in the clinic. These data can then help inform PACTs of best practices, falling into alignment with precision medicine.
- Participation on the IPRCC NPS: The IOM recommended the "Secretary of the Department of Health and Human Services (DHHS) should develop a comprehensive population health-level strategy for pain prevention, treatment, management, education, reimbursement, and research that includes specific goals, actions, time frames, and resources." As a result, the IPRCC was tasked by DHHS with developing an NPS as outlined by the IOM. A plan was developed by IPRCC members to accomplish this goal, including an oversight committee and thematic working groups responsible for creating a draft plan for the respective theme. The breadth of expertise provided by VA investigators is evidenced by participation on the working groups and includes Professional Education and Training—Dr. Rollin "Mac" Gallagher; Public Education and Communication—Drs. Keith Humphreys and John Piette; Disparities—Dr. Diana J. Burgess; Service Delivery and Reimbursement—Drs. Karl Lorenz, Patricia Sinnott, and Robert D. Kerns (who also participated as a member of the NPS Oversight Committee); and Population Research—Dr. Joseph L. Goulet. Much time, effort, and collegiality was needed to create a draft of the NPS that was posted on the IPRCC Web site and the Federal Register for public input. The NPS is now in its final stages of amendment prior to final approval by all Federal agencies represented on the IPRCC.

VA's research programs are unique entities, serving as platforms and resources for the research community and the Veterans we serve. The programs I have highlighted are only a small sample of the great research VA investigators are conducting and demonstrates that our investigators are viewed as experts by the pain research community. It can be concluded that we are experiencing "growing pains," but this kind of

meetings and frequent presentations by members of the PRWG. This regular communication conveys several key benefits to VHA pain research. It enables the perpetuation of a close working relationship between the PRWG and the National Pain Management Program Office in Central Office, ensuring that VHA pain research is informed by the clinical needs of our Veterans and the policy needs for their health services as well as effective partnerships between our office and investigators in the field.

VHA's pain research enterprise addresses our society's important need for implementation research, a recognized "donut hole" of the National Institutes of Health research portfolio. Our clinical and administrative database, built on the electronic health record, enables studies of larger trends in care, variability in care, and the effects of larger scale practice interventions and policy changes, as well as epidemiologic studies that inform hypotheses for prospective studies, clinical trials, and implementation research. Moreover, the need for translational research leading to effective biologic treatments with lesser toxicities that can be paired with neurobehavioral therapies has never been greater. The future is bright for VHA pain research.

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VHA PAIN RESEARCH WORKING GROUP AND VHA PAIN CARE

Rollin M. Gallagher, MD, MPH

This important special issue of the *Journal of Rehabilitation Research & Development* (*JRRD*) documents the steady progress of the Veterans Health Administration (VHA) in promoting and supporting pain research. As described by Drs. Kerns and Heapy in their Editorial [1], the development of the VHA's pain research enterprise has evolved over many years, with a particular focus on understanding the factors, including combined treatments, that affect the course and outcome of pain care for Veterans and inform clinical policy. The articles herein provide a sample of the breadth and sophistication of the VHA pain research enterprise in several domains: observational studies that help us understand the biopsychosocial factors influencing the development and perpetuation of chronic pain and pain treatment outcomes in Veterans with chronic pain and its comorbidities, such as posttraumatic stress disorder; investigations of the effects of exercise on pain sensitivity; and studies of the efficacy of multimodal treatments, e.g., combining exercise with medications to improve physical capacity.

Our clinical and administrative database, built on the electronic health record, enables studies of larger trends in care, variability in care, and the effects of larger scale practice interventions and policy changes, as well as epidemiologic studies that inform hypotheses for prospective studies, clinical trials, and implementation research.

An important nidus of the VHA's effort lies in the Pain Research Working Group (PRWG), led by Dr. Kerns, which has met by telephone monthly for many years and in face-to-face meetings in several venues. These meetings have served to enable dialog between officials from the VHA's Office of Research Development (ORD) with pain investigators, to introduce new investigators to the VHA pain research enterprise, and to foster collaborations among VHA investigators and research centers. Meetings of the PRWG in several retreats and, in recent years, at the yearly Health Services Research & Development (HSR&D) meetings have enabled the interpersonal connectivity so critical to social networking in the development of a multicenter research enterprise. As an example, the VHA Center for Healthcare Equity Research and Promotion based at my VHA institution, the Philadelphia Department of Veterans Affairs (VA) Medical Center, supported a PRWG retreat chaired by Dr. Kerns in 2005, when I was new to the VHA, that led to my connection to VHA's Rehabilitation Research & Development Service (RR&D) and my subsequent research, education, and policy work with the Department of Defense and with several VHA investigators. The RR&D-sponsored pain state-of-the-art research conference in September 2007, focusing on Veterans of the wars in Iraq and Afghanistan and chaired by Dr. Kerns, led to a special issue on VHA pain research in *Pain Medicine* in 2009, co-edited by Dr. Kerns and pain research leader Dr. Steve Dobscha from Oregon [2].

Dr. Kerns' extraordinary leadership in encouraging, sustaining, and expanding VHA pain research over these many years, which has been strongly supported by Dr. Kusiak and VHA ORD as well as VHA Central Office leadership, has been accompanied by a steady growth in the pain research enterprise throughout VHA. A recent highlight is the HSR&D-funded Center of Innovation (COIN) at the VA Connecticut Healthcare System, called the Pain Research, Informatics, Multi-Morbidities, and Education (PRIME) Center led by Drs. Kerns, Heapy, and others, which convenes research experts from around VHA to focus on pain research and complements other VHA centers that, although not exclusively devoted to pain research, have developed important pain research programs. Of particular note is research at the primary care level that has provided support for the Stepped Care Model [3–8]. Following the COIN award, Dr. Kerns' administrative leadership of the National VHA Pain Management Program Office naturally evolved to his present position as Special Advisor for Pain Research to our office, which involves his participation in our weekly pain management office

meetings and frequent presentations by members of the PRWG. This regular communication conveys several key benefits to VHA pain research. It enables the perpetuation of a close working relationship between the PRWG and the National Pain Management Program Office in Central Office, ensuring that VHA pain research is informed by the clinical needs of our Veterans and the policy needs for their health services as well as effective partnerships between our office and investigators in the field.

VHA's pain research enterprise addresses our society's important need for implementation research, a recognized "donut hole" of the National Institutes of Health research portfolio. Our clinical and administrative database, built on the electronic health record, enables studies of larger trends in care, variability in care, and the effects of larger scale practice interventions and policy changes, as well as epidemiologic studies that inform hypotheses for prospective studies, clinical trials, and implementation research. Moreover, the need for translational research leading to effective biologic treatments with lesser toxicities that can be paired with neurobehavioral therapies has never been greater. The future is bright for VHA pain research.

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JRRD at a Glance

Pain research using Veterans Health Administration electronic and administrative data sources

Erica A. Abel, PhD, et al.

Pain researchers may use electronic health records and other Veterans Health Administration (VHA) data sources to examine the prevalence, treatment, effect, and outcomes of pain and pain management in Veterans. This article presents the results of a survey of pain researchers. We asked about their experiences with, opinions about, confidence in, and perceived barriers to using VHA data sources. Most of those surveyed reported using VHA data sources. Less than half thought the sources were adequate for pain research. Despite some challenges, pain researchers are using VHA data sources to improve healthcare services for Veterans with pain.

http://dx.doi.org/10.1682/JRRD.2014.10.0246

Association between pain outcomes and race and opioid treatment: Retrospective cohort study of Veterans

Diana J. Burgess, PhD, et al.

Previously, we found rates of opioid prescriptions to be lower among black versus white Department of Veterans Affairs primary care patients with a diagnosis of chronic noncancer pain. In this study, we found that these racial differences in opioid prescription were not associated with poorer pain outcomes for black patients; receipt of an opioid prescription was generally not associated with perceptions of treatment effectiveness and was associated with greater pain interference for both white and black Veterans. Findings raise questions about the benefits of opioids for chronic pain, in light of the risks, and point to the need for alternative treatment approaches.

http://dx.doi.org/10.1682/JRRD.2014.10.0252

Correlates of prescription opioid therapy in Veterans with chronic pain and history of substance use disorder

Travis I. Lovejoy, PhD, MPH, et al.

This study characterized opioid prescription in a sample of Veterans Health Administration patients with chronic pain and lifetime substance use disorder histories. Participants prescribed long-term opioid therapy had a greater number of pain diagnoses and endorsed poorer pain-related function than those not prescribed opioid therapy or those prescribed short-term opioid therapy. Findings highlight the poor pain-related functioning in patients with history of substance use disorder who are prescribed long-term opioid therapy.

http://dx.doi.org/10.1682/JRRD.2014.10.0230

Does comorbid chronic pain affect posttraumatic stress disorder diagnosis and treatment? Outcomes of posttraumatic stress disorder screening in Department of Veterans Affairs primary care

Samantha D. Outcalt, PhD, et al.

Department of Veterans Affairs primary care clinics routinely perform screening tests for posttraumatic stress disorder (PTSD). It is important to understand what happens after a Veteran screens positive for PTSD in primary care. This study examined how comorbid chronic pain could affect this process. We examined 4,244 primary care patients with a positive PTSD screen and compared outcomes based on whether they also had a pain diagnosis. We found that patients with coexisting pain had a slightly lower rate of mental health visits than those without pain. There were no differences in rates of PTSD diagnosis or new antidepressant medication prescription.

http://dx.doi.org/10.1682/JRRD.2014.10.0237

Fibromyalgia syndrome care of Iraq- and Afghanistan-deployed Veterans in Veterans Health Administration

April F. Mohanty, MPH, PhD, et al.

Among Iraq- and Afghanistan-deployed Veterans, 1 percent were diagnosed with fibromyalgia syndrome. Most had combined care (defined as regular primary care combined with mental health and/or rheumatology specialty care visits), which can be important for expert management of fibromyalgia syndrome and common comorbidities. Combined care is a recommended practice, but in our sample, it was associated with greater likelihood of prescription of opioid medications, which is not a recommended treatment for fibromyalgia syndrome. Combined care was also associated with greater likelihood of prescription of nonopioid pain medications. These results indicate possible benefits of combined care but also reflect the probable greater complexity of Veterans receiving combined care.

http://dx.doi.org/10.1682/JRRD.2014.10.0265

Iraq and Afghanistan Veterans report symptoms consistent with chronic multisymptom illness one year after deployment

Lisa M. McAndrew, PhD, et al.

We used data from a prospective longitudinal study of Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) Veterans to determine the frequency of symptoms consistent with chronic multisymptom illness (CMI). CMI is characterized by multiple chronic symptoms. We found that 1 yr postdeployment, 49.5 percent of OIF/OEF Veterans met criteria for mild to moderate CMI and 10.8 percent met criteria for severe CMI. Veterans with symptoms consistent with CMI reported significantly worse physical health function than Veterans who did not report symptoms consistent with CMI. This study suggests that the presence of CMI should be considered in the evaluation of OIF/OEF Veterans.

http://dx.doi.org/10.1682/JRRD.2014.10.0255

Prevalence and correlates of painful conditions and multimorbidity in national sample of overweight/obese Veterans

Diana M. Higgins, PhD, et al.

Chronic pain and overweight/obesity occur at particularly high rates among Veterans in Veterans Health Administration care. To better understand the overlap of these conditions and the effect of additional medical and mental health conditions on these co-occurring conditions, we examined rates of back pain and arthritis among a national sample of Veterans with overweight/obesity. A majority of these Veterans (72%) reported back and/or arthritis pain. Women Veterans were more likely to report arthritis and combined back pain and arthritis. Veterans who reported pain were more likely to report additional health conditions, which may make treating co-occurring overweight/obesity and chronic pain more challenging.

http://dx.doi.org/10.1682/JRRD.2014.10.0251

Sex differences between Veterans participating in interdisciplinary chronic pain rehabilitation

Jennifer L. Murphy, PhD, et al.

The purpose of this research study was to see whether differences existed between male and female Veterans who took part in a residential treatment program for chronic pain. We looked at differences in how they changed during and after the program. The results indicate that some differences existed in the men and women who participated in the treatment and in how they benefitted. Since the number of women using the Department of Veterans Affairs for their healthcare is rising, this research helps to understand who may choose to participate in programs for chronic pain and how to adjust their pain treatment.

http://dx.doi.org/10.1682/JRRD.2014.10.0250

Potential neurobiological benefits of exercise in chronic pain and posttraumatic stress disorder: Pilot study

Erica Scioli-Salter, PhD, et al.

Individuals with both chronic pain and posttraumatic stress disorder (PTSD) may experience greater pain, distress, and disability than if they have either condition alone. Research indicates that individuals with pain and/or PTSD may have abnormally low levels of the antistress, antinociceptive hormones neuropeptide Y (NPY) and allopregnanolone and pregnanolone (together termed ALLO) and that exercise may help to increase these levels. This study investigated how cortisol, dehydroepiandrosterone, NPY, and ALLO respond to a maximum load exercise stress test in relation to pain sensitivity in a group of trauma-exposed men and women with and without PTSD and chronic pain. Both NPY and ALLO levels correlated with cardiorespiratory fitness, as well as with pain threshold and tolerance, respectively. The findings suggest that improving fitness through exercise training may reduce pain sensitivity in this population.

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Opioid use and walking among patients with chronic low back pain

Sarah L. Krein, PhD, RN, et al.

Managing chronic back pain, a common problem among Veterans, is a significant challenge. Opioid medications are frequently used to manage pain, but this is of concern because of documented problems with their safety and effectiveness. However, whether patients who receive opioids might engage in other recommended forms of therapy, such as physical activity, is unknown. Our study findings suggest that with additional support, patients taking opioids may engage in walking to help manage their back pain, emphasizing the importance of encouraging the use of alternative pain management strategies for these patients.

http://dx.doi.org/10.1682/JRRD.2014.08.0190

Perceptions of other integrative health therapies by Veterans with pain who are receiving massage

Carol Elizabeth Fletcher, PhD, RN, et al.

Veterans are seeking complementary and integrative health (CIH) therapies in addition to conventional care for issues such as chronic pain and posttraumatic stress disorder. In response, the Department of Veterans Affairs (VA) has begun offering therapies such as massage and yoga, but as with any new program there are challenges. Veterans benefit when other Veterans describe their experiences to clarify the successes and problems that Veterans have when obtaining, or trying to obtain, CIH therapies through the VA. Understanding Veterans' experiences is essential if the VA wishes to successfully provide CIH therapies to Veterans.

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Initial development of a patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy

William C. Becker, MD, et al.

We identified a need for a comprehensive, feasible, and clinically actionable instrument to monitor long-term opioid therapy in primary care, where most opioids are prescribed. The present study describes the initial development steps of a preliminary version of such an instrument, the Patient Reported Indications for Opioid Reassessment (PRIOR). Forty-seven subject matter experts in the clinical field of long-term opioid therapy highly rated 37 items related to harm, efficacy, and misuse. These items were modified and tested for Veteran comprehension in this study developing the preliminary PRIOR.

http://dx.doi.org/10.1682/JRRD.2014.11.0285

Stepped care model for pain management and quality of pain care in long-term opioid therapy

Brent A. Moore, PhD, et al.

The Pain Care Quality (PCQ) extraction tool was used to examine the effect of interventions to improve primary care provider's quality of pain care. The study examined electronic health records of patients receiving opioid medication in one Veterans Health Administration (VHA) healthcare system over 4 years and a non-VHA Federally qualified health center over 2 years. Documentation of reassessment of pain and pain education improved in the VHA. Results suggest that the PCQ extraction tool is feasible and may be responsive to change in the context of efforts to promote organizational improvements in pain care of Veterans.

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Implementation of telementoring for pain management in Veterans Health Administration: Spatial analysis

Evan P. Carey, MS, et al.

In 2011, the Veterans Health Administration (VHA) started a telementoring program called the Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO) for pain management in seven healthcare networks. This analysis examines the implementation of Pain SCAN-ECHO by mapping the location of Veterans with chronic pain, VHA healthcare resources, and the reach of the program in a sample network. For all seven networks, we investigated the relationship between distance to nearest in-person specialty pain care and access to a primary care provider participating in Pain SCAN-ECHO.

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Pain research using Veterans Health Administration electronic and administrative data sources

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Abstract—Health services researchers are using Veterans Health Administration (VHA) electronic health record (EHR) data sources to examine the prevalence, treatment, and outcomes of pain among Veterans in VHA care. Little guidance currently exists on using these data; thus, findings may vary depending on the methods, data sources, and definitions used. We sought to identify current practices in order to provide guidance to future pain researchers. We conducted an anonymous survey of VHA-affiliated researchers participating in a monthly national pain research teleconference. Thirty-two researchers (89%) responded: 75% conducted pain-focused research, 78% used pain intensity numeric rating screening scale (NRS) scores to identify pain, 41% used International Classification of Diseases-9th Revision codes, and 57% distinguished between chronic and acute pain using either NRS scores or pharmacy data. The NRS and pharmacy data were rated as the most valid pain data sources. Of respondents, 48% reported the EHR data sources were adequate for pain research, while 45% had published peer-reviewed articles based on the data. Despite limitations, VHA researchers are increasingly using EHR data for pain research, and several common methods were identified. More information on the performance characteristics of these data sources and definitions is needed.

Key words: administrative data, computerized medical records, data collection, data interpretation, data mining, electronic health records, information storage and retrieval, pain, pain management, Veterans.

INTRODUCTION

The Veterans Health Administration (VHA) uses an electronic health record (EHR) to collect clinical and administrative data. Because the VHA is a national

Abbreviations: CAHPS = Consumer Assessment of Healthcare Providers and Systems, CDW = Corporate Data Warehouse, CPRS = Computerized Patient Record System, EHR = electronic health record, HAIG = Health Analysis and Information Group, HERC = Health Economics Resource Center, HSR&D = Health Services Research and Development Service, ICD-9 = International Classification of Diseases-9th Revision, MCA = Managerial Cost Accounting, MedSAS = Medical SAS, NEPEC = Northeast Program Evaluation Center, NPCD = National Patient Care Database, NRS = pain intensity numeric rating screening scale, OIF/OEF = Operation Iraqi Freedom/Operation Enduring Freedom, PRWG = Pain Research Working Group, PTF = Patient Treatment File, PTSD = posttraumatic stress disorder, RAI/MDS = Resident Assessment Instrument/Minimum Data Set, SHEP = Survey of Healthcare Experiences of Patients, VA = Department of Veterans Affairs, VHA = Veterans Health Administration, VIReC = VA Information Resource Center, VistA = Veterans Health Information Systems and Technology Architecture.

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integrated healthcare system that serves a diverse population of over 8 million Veterans per year in more than 140 facilities [1], EHR-based data can potentially provide valuable information on a variety of healthcare-related issues.

Researchers have successfully used EHR and administrative data in different ways. Such data have been used to create condition-specific registries [2], conduct data quality evaluations [3], differentiate the severity of mental health and medical conditions [4], describe longitudinal health services utilization [5], study outcomes [6], and improve the quality of care [7]. Within VHA, researchers have used EHR and administrative data to examine a diverse array of issues [8] such as mental health [9–11], human immunodeficiency virus [12–13], women's Veterans health [14], sex differences [15–16], diabetes [17–18], and stroke [19–20].

Pain is one of the most common reasons for seeking medical care [21], and health services researchers are using VHA EHR data sources to examine the prevalence, treatment, effect, and pain management practices among Veterans in VHA care. For example, Sinnott et al. evaluated several methods for identifying individuals with neck and back pain [22]. They identified seven unique published algorithms and outlined the similarities and differences in the structure and definitions of the algorithms. They then assessed and compared the algorithms by applying them to VHA administrative data (e.g., Patient Treatment Files [PTFs] for inpatient data and the National Patient Care Database [NPCD] for outpatient data). Lisi et al. compared VHA administrative data and structured chart review and identified and tested methods to distinguish between acute and chronic nonacute lower back pain among Veterans [4]. Models they constructed included several variables in addition to International Classification of Diseases-9th Revision (ICD-9) codes (e.g., prescriptions, consultations, and imaging orders). Variables were extracted from several Veterans Health Information System and Technology Architecture (VistA) databases and files (VistA stores EHR data).

Haskell et al. evaluated sex differences in the prevalence of overall pain, moderate to severe pain, persistent pain, and pain assessment in a cohort of Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) Veterans seen at an outpatient VHA clinic in the first year after their last deployment [15]. The researchers obtained demographic and military service information from the OIF/OEF roster, a database of Veterans who have separated from military service and have enrolled in VHA healthcare. The source of the roster is the Defense Manpower Data Center [23]. Visit information, ICD-9 codes, and pain intensity numeric rating screening scale (NRS) scores were obtained from the Corporate Data Warehouse (CDW).

Goulet et al. examined the degree of agreement between EHR-based and patient survey-based NRS scores and examined factors that could explain discrepancies [24]. Finley et al. studied the association of the polytrauma clinical triad (the co-occurrence of posttraumatic stress disorder [PTSD], traumatic brain injury, and chronic pain) with suicide-related behavior risk among OIF/OEF Veterans [8]. They identified Veterans using the OIF/OEF roster and used administrative data (e.g., VHA inpatient and outpatient data) to identify baseline characteristics (e.g., ICD-9 codes) and outcomes (e.g., suicide ideation, attempted or self-inflicted injury) [8]. Using a cohort of OIF/OEF Veterans, Seal et al. investigated the association of mental health disorders, in particular PTSD, on patterns of opioid prescription use and adverse clinical outcomes such as overdose and accidents [25]. VHA data sources used included the OIF/OEF roster, clinical visit and diagnostic information, and pharmacy records.

These studies highlight the variety of methods, definitions, and data sources used in pain-related research. While there are different approaches to using VHA EHR and administrative data, factors such as the inherent structure of VHA data (i.e., the large number of available data sources and data elements) and the existence of different relevant data owners and procedures to gain access to data sources can affect research results. Thus, research findings can vary depending on the methods and sources of data that researchers use to identify samples of patients and to define outcomes. For example, some may approach the identification of patients with pain through pharmacy dispenses of opioid medications, by NRS scores of a certain threshold (e.g., ≥4 to indicate moderate to severe pain), by ICD-9 code, or through a combination thereof. Different definitions can contribute to pain researchers arriving at very different conclusions.

The use of EHR data, originally collected for clinical and administrative purposes and not research purposes, highlights the importance of establishing how best to use the available data to conduct pain-related research. As a first step toward establishing best practices to leverage optimal use of VHA EHR data, we conducted an anonymous survey of VHA-affiliated pain researchers. The survey results were intended to serve as a basis for future

efforts to derive a consensus about recommended data sources, definitions, and methods to aid researchers in conducting studies that are comparable and consistent and ultimately to help improve healthcare services for Veterans.

The survey asked about respondents' research focuses, how they defined certain concepts (e.g., pain, acute and chronic pain), and whether they used a comparison or control group in their most recent research. We asked which specific national data sources they used in their pain research, which sources they used to identify the presence of pain, and how valid they felt the sources were. We inquired about potential barriers to data use, whether VHA data were adequate for pain research, and whether the respondents would be willing to participate in an expert panel to discuss issues and recommendations for pain research using VHA data.

METHODS

Participants

In 2012, all active members (n = 36) of the national VHA Pain Research Working Group (PRWG) were invited to participate in a voluntary, one-time, online survey about their use of VHA EHR and administrative data in pain-related research. The PRWG was created to support a key objective of the VHA National Pain Management Strategy: "Identifying research opportunities and priorities in pain management and facilitating collaborative research efforts" [26]. Members of the group include VHA investigators as well as collaborating investigators outside of the VHA. The Department of Veterans Affairs (VA) Connecticut Healthcare System Human Subjects Subcommittee approved this investigation.

The study principal investigator (J.G.) sent an email announcement to the group using a preexisting email distribution list as a source for names. Email messages were sent once a month for 3 mo (totaling three emails) to all group members, inviting respondents' voluntary and anonymous participation in an online survey. Respondents used REDCap (Research Electronic Data Capture) [27], a secure, Web-based application designed to support data capture for research studies, to complete the survey. No names or personally identifying information about either respondents or VHA patients were collected. Rather, the survey asked about primary affiliation, professional discipline, primary service department, pain research focus, and use and opinions of VHA EHR and administrative data.

Survey Questions

See the **Appendix** (available online only) for the survey questions used in this study.

Data Source Use and Validity

We asked survey respondents to indicate whether they used any of eight EHR and administrative data sources that have been used in other areas of research and to rate their opinion of the validity of the source on a scale of 1 (not valid) to 7 (valid).

Most Recent Research

We asked seven questions about respondents' most recent research, including several dichotomous "yes/no" questions, such as whether they distinguished between chronic and acute pain, used a comparison or control group, or examined recurrence of pain. We then asked open-ended questions about how they defined pain and chronic pain and asked them to identify the geographic area (e.g., national or local VHA facility only) of their most recent research. Finally, we asked whether respondents had ever published any pain-focused peer-reviewed articles.

Barriers to Data Source Use

We asked respondents about barriers to their use of VHA electronic and administrative data. We provided a list of 10 known barriers (plus an option for "none"). We compiled the list of barriers based on the combined experience of authors (J.G., C.B.) who have developed three large VHA data cohorts. Respondents could also add any additional barriers not listed. We also asked them to rate each barrier, including ones the respondents added, as a "minor barrier," "major barrier," or "not a barrier."

Adequacy of Data for Pain Research

Survey respondents were asked the following question to ascertain their opinion of the adequacy of data sources for pain research: "Do you think VHA electronic and administrative data are adequate for pain research?" Single questions were then asked to elicit feedback about (1) how respondents would improve VHA electronic and administrative data for pain research and (2) whether respondents would be interested in participating in an expert panel to discuss issues in pain research using VHA data.

Data Sources and Definitions

There are approximately 139 data sources within VHA [28]. Given this sizeable number of data sources potentially available to conduct pain research, we felt it would be useful to identify and ask respondents about a subset of those sources often used in pain research. We relied on our prior experience conducting pain research and the prior publications of VHA pain-related researchers to identify the subset and describe them here for clarity and informational purposes. Hynes provides information about many of these resources and gaining access to them [28].

Corporate Data Warehouse

The CDW is a national repository of VHA clinical and administrative data [29]. Data include national clinical, enrollment, financial, administrative, utilization, and benefits information consolidated from multiple VHA data sources. The CDW allows for a standardized database structure and facilitates analysis and reporting.

Veterans Health Administration Medical SAS Inpatient and Outpatient Data Sets

The Medical SAS (MedSAS) inpatient and outpatient data sets consist of national VHA healthcare encounter data, specifically workload information at the encounter, visit, or stay level, for inpatient and outpatient healthcare encounters. MedSAS inpatient data are obtained from the PTF and both the outpatient and inpatient encounter MedSAS data are taken from the NPCD [30]. The NPCD is a centralized database of integrated patient care data from VistA.

Department of Veterans Affairs Managerial Cost Accounting System

The Managerial Cost Accounting (MCA) system (formerly known as the Decision Support System) is a cost allocation system that can generate the costs of healthcare use for hospital stays and outpatient care at an individual patient level. Examples of data reported include costs of ordering chest X-rays, clinic visits, and inpatient visits [31].

Beneficiary Identification and Records Locator System Death File

The Beneficiary Identification and Records Locator System death file is a Veterans Benefits Administration-extracted death file database that contains cumulative information about Veterans' deaths. This database is compiled from multiple sources such as VHA hospitals, family members applying for benefits, the VA National Cemetery Administration, and the Social Security Administration.

National Surgical Quality Improvement Program

The National Surgical Quality Improvement Program includes risk-adjusted data extracted from patient charts and provides preoperative to postoperative patient outcomes.

Pharmacy Benefits Management

Pharmacy Benefits Management is a comprehensive national database containing information about all prescriptions dispensed at a VHA pharmacy or consolidated mail outpatient pharmacy since fiscal year 1999. Data include "medication dispensing utilization information for prescription fills in VHA pharmacies" [32], dosing instructions, National Drug Code identifiers, cost, and provider information.

Survey of Healthcare Experiences of Patients

The Survey of Healthcare Experiences of Patients (SHEP) is a VHA survey program that assesses patient experiences with inpatient and outpatient healthcare with the overall goal of improving the quality of VHA healthcare. In 2010, the SHEP program began using the Agency for Healthcare Research and Quality's Consumer Assessment of Healthcare Providers and Systems (CAHPS) family of survey instruments. As developed, these surveys are standardized and thus comparable across settings, and their psychometric properties are well-documented [33]. The SHEP program implements additional CAHPS survey instruments in accordance with VHA priorities.

Health Analysis and Information Group Pain Management Survey Data

The Health Analysis and Information Group (HAIG) pain management survey data include a comprehensive field-based survey of pain management in all VHA facilities conducted in 2009 by the HAIG in collaboration with the Pain Management Program Office. All facilities responded, and the role of respondents varied by facility (e.g., pain management point of contact or not). Available data include adherence to VHA pain management directive, clinical care characteristics, pain management

stepped care model implementation, and focused review of specific priority areas.

Bar Code Medication Administration

The Bar Code Medication Administration is a VistA module that provides inpatient medication dispensing safety and control to reduce inpatient medication errors. It does so by electronically validating and documenting medications for patients. The system visually alerts clinicians when medication-dispensing conditions are not met.

Department of Veterans Affairs Resource Centers

We included in the survey four of the eight national VA resource centers that are commonly used by VHA pain researchers. We selected these four sources by drawing on our experience as pain researchers.

Serious Mental Illness Treatment Resource and Evaluation Center

The Serious Mental Illness Treatment Resource and Evaluation Center is a VA Health Services Research and Development Service (HSR&D) research center that develops and maintains two national data repositories: the National Psychosis Registry and the National Registry for Depression [34].

Health Economics Resource Center

The Health Economics Resource Center (HERC) is an HSR&D resource center that provides data about VHA facility, departmental, and individual healthcare costs, specifically inpatient and outpatient costs along with fee basis or costs related to outside care with a provider contracted with VHA. HERC also produces several resources, including MCA cost data [35].

Department of Veterans Affairs Information Resource Center

The VA Information Resource Center (VIReC) is an HSR&D resource center that develops and disseminates knowledge about data resources and provides guidance and assistance to researchers [31]. VIReC also provides access to VA and Centers for Medicare and Medicaid Services data, including United States Renal Data System data.

Northeast Program Evaluation Center

The Northeast Program Evaluation Center (NEPEC) is the evaluation division of the National Center for PTSD [36]. NEPEC is responsible for evaluating Office of Mental Health services programs, including PTSD clinical programs.

RESULTS

Of 36 researchers contacted, 32 (89%) respondents completed the survey. Nearly all (94%) identified their primary affiliation as VHA. Respondents included psychologists (33%), physicians (25%), epidemiologists (13%), and statisticians (13%). Seventy-two percent reported conducting research in an outpatient setting, and 44 percent identified chronic pain as their primary area of research. The majority of respondents (75%) had been a principal investigator or co investigator on pain-focused studies. Two-thirds (67%) reported they had received VHA funding for their most recent pain-related research, 25 percent reported they had received funding from "other" sources, and 8 percent reported they had received National Institutes of Health funding. No respondents reported Department of Defense funding.

As shown in **Table 1**, more respondents endorsed using NRS scores (78%), ICD-9 codes for pain (66%), and/or Computerized Patient Record System (CPRS) progress notes (41%) to identify the presence of pain than other data sources. Respondents' impressions of the validity of the sources of pain data were highest for

Table 1.
Sources of pain data.

Source	Percent*	Impression of Data Validity (median score)†
NRS Scores	78	5
ICD-9 Codes for Pain	66	4
CPRS Progress Notes	41	4
Pharmacy	39	5
CPT Codes	38	4
CPRS Problem List	38	3.5
Other (e.g., patient self-report, RAI/MDS)	24	5.5
Clinic Stop Codes	22	4
CPRS Discharge Summary	16	4

*Individuals could endorse multiple sources and thus numbers do not sum to 100%.
†Range = 1 (not valid) to 7 (valid).
CPRS = Computerized Patient Record System, CPT = Current Procedural Terminology, ICD-9 = International Classification of Diseases-9th Revision, NRS = pain intensity numeric rating screening scale, RAI/MDS = Resident Assessment Instrument/Minimum Data Set.

"other" (including patient self-report and the Resident Assessment Instrument/Minimum Data Set [RAI/MDS]), NRS scores, and pharmacy sources.

In their most recent research, 41 percent of respondents reported they relied on ICD-9 codes only and 21 percent of respondents used NRS scores only to define pain. More than half of the respondents (57%) distinguished between chronic and acute pain.

Among those who reported how they defined chronic pain, most reported using NRS scores of ≥4 during some interval of time. Nearly one-third of the respondents (32%) constructed a comparison or control group, 25 percent had a national focus, 13 percent had a Veterans Integrated Service Network focus, and 16 percent had a local facility focus. Less than half (45%) reported they published pain-focused peer-review articles using VHA electronic and administrative data.

We ascertained respondents' perceived barriers to the use of VHA electronic and administrative data for pain-related research. As shown in **Table 2**, "insufficient level of detail in data" received the greatest percentage of endorsements as a major barrier (33%). The other identified major barriers included "data management issues (e.g. cleaning data)" and "data quality (e.g. completeness, lack of validation)" (both 27%) and "privacy/ Health Insurance Portability and Accountability Act concerns" (23%). Two factors received the greatest percentage of endorsements as "not a barrier": "timeliness of data" (77%) and "lack of hardware to house data (e.g., computer storage)" (73%).

Regarding use of VHA data sources, as shown in **Table 3**, less than half (44%) of the respondents reported using the VHA's integrated data warehouse (CDW) or the MedSAS data sets (47%). Of note, despite the evident use of VHA data sources by these researchers, only 48 percent thought that the data sources were adequate for pain research. More than half of respondents (58%) said they would be willing to participate in an expert panel to discuss issues in pain research using VHA data.

DISCUSSION

The results of this survey provide insight into how VHA pain researchers use VHA EHR and administrative data to conduct pain-related research. Nearly half of the respondents did not think VHA EHR and administrative data were adequate for pain research. Despite limitations in these data sources, pain researchers are using them and in different ways. The survey results also showed variations in key approaches to pain research, including which specific data sources were used, how chronic pain was defined, how chronic and acute pain were distinguished, whether a comparison or control group was used, and perceived barriers to using such data sources for pain research.

The majority of respondents endorsed using the NRS scores and/or ICD-9 codes. The NRS is a brief instrument, is easy to administer, correlates with other pain intensity measures, and is widely used in large healthcare settings and research. Thus, NRS scores may be relatively easier to obtain from EHR and administrative data relative to other pain data. While this survey result is similar to published literature, there are issues with reliance on NRS scores. They do not describe important

Table 2.
Barriers to use of Veterans Health Administration electronic and administrative data for pain research.

Barrier	Not a Barrier (%)	Major Barrier (%)	Minor Barrier (%)
Insufficient Level of Detail in Data	7	33	60
Data Management Issues (e.g., cleaning data)	10	27	63
Data Quality (e.g., completeness, lack of validation)	13	27	60
Privacy/HIPAA Concerns	27	23	50
Inability to Access Data	17	20	63
Lack of Expertise in Analyzing Data	53	17	30
Data Security	50	10	40
Timeliness of Data	77	7	17
Lack of Hardware to House Data (e.g., computer storage)	73	3	23
Lack of Standardization (e.g., site variation)	27	3	23

Note: Individuals could endorse multiple resources and thus numbers do not sum to 100%.
HIPAA = Health Insurance Portability and Accountability Act.

Table 3.
Top five Veterans Health Administration resources used in pain research.

Resource	Percent
Medical SAS Data sets	47
Corporate Data Warehouse	44
Decision Support System	28
Beneficiary Identification and Records Locator System Death File	22
Survey of Healthcare Experiences of Patients	16

information (e.g., persistence of pain, level of impairment), and they may underestimate direct patient reports of pain [24].

ICD-9 codes are assigned to and available for most inpatient and outpatient encounters, are captured in EHR and administrative data, and thus are relatively easy to access. However, they are often used for purposes that are a departure from their original intent [37], and their accuracy in identifying patients with specific conditions is variable. Because of reliability and validity issues using ICD-9 codes to identify patients, including those with pain [38], researchers have developed identification algorithms to improve accuracy (e.g., using a specific number of inpatient and/or outpatient ICD-9 codes within a given time frame) [12,38]. Pain researchers have developed and evaluated identification algorithms that use ICD-9 codes (along with other data) to identify patients with pain [4,6–7,22].

Our survey results suggest that VHA pain researchers use EHR and administrative data sources and recognize and capitalize on their advantages for research. VHA EHR and administrative data sources contain information on a large and diverse sample of individuals, and much of the data are entered or stored in structured fields. Researchers may be able to evaluate treatment outcomes using observational designs across a wider range of clinical settings, geographical regions, and patients and have access to samples of patients in preparation for recruitment for clinical trials [2] and/or survey studies. Use of EHR and administrative data for research may also be less expensive and time-consuming than studies that require patient recruitment and/or data collection [39]. In addition, use of existing data may reduce participant risk (e.g., reduce study intervention risk) and participant burden (e.g., eliminate the burden or expense of traveling to participate in a research study or time needed to complete a protocol). The variability in the methods, data sources, and definitions used by survey respondents may also reflect these advantages of EHR and administrative data, including the potential for greater flexibility in designing and executing research.

This survey highlights some of the known limitations to using EHR and administrative data for research. Because these sources are designed and implemented to support patient care and clinical processes, not research [40], the data needed to accomplish research objectives may not be available, may lack the information and details needed, or may be hard to retrieve. For example, EHR and administrative data omit valuable information [2], such as the severity of a patient's illness [30] and degree of disability. In addition, important information and details may be embedded in text format (e.g., clinician progress notes, secure email messages, and texts from patients) and thus are harder to retrieve and analyze than structured data.

Survey respondents appear to recognize these limitations as evidenced in their endorsement of both "insufficient level of detail in data" and "data quality (e.g., completeness, lack of validation)" as two major barriers to use of VHA EHR and administrative data. These limitations may also explain why survey respondents endorsed greater usage of NRS scores, ICD-9 codes, and CPRS progress notes to identify the presence of pain. Respondents may be less likely to use data they consider to have the highest validity (i.e., patient self-report and RAI/MDS), because this information is not available, is difficult to ascertain on a large scale (e.g., patient self-report), or is available for a specific population such as patients in nursing homes (e.g., RAI/MDS) or a limited number of patients (e.g., study-specific surveys). Respondents appear to want more in-depth data about pain (such as the PEG instrument [41]) in VHA EHR and administrative data and may be using NRS scores, ICD-9 codes, and CPRS progress notes in the absence of more detailed and better data.

The lack of standardization over time of EHR and administrative data is another significant challenge. Specific databases may have been developed and implemented in response to distinct administrative, operational, quality improvement, or clinical needs and may be incompatible with national or organizational standards. The data rules, definitions, and structures may be unique to each legacy system [42], and the data may have been obtained, entered, and stored differently. Data may need to be merged, which may be an added challenge. The VHA has encountered these problems and has approached the

challenges presented by its legacy systems, unconsolidated data, and multiple databases by implementing the CDW because attempts to apply common standards across legacy systems were impractical. Essentially, it was more practical and efficient to create a vast, modern data structure and repository than to attempt to modernize or to redesign historic systems.

In addition to its focus on improving data and systems, VHA is increasingly focused on data users. There are valuable, user-focused resources such as the VHA data portal (an online gateway to VHA data information, resources, and training), VIReC (a resource center designated to provide guidance to VHA researchers using data), and VA Informatics and Computing Infrastructure (an environment that provides researchers access to analytical tools and clinical and administrative data sets). User-focused resources such as these facilitate practical access to data, knowledge about and use of available data sources, and project collaboration so that individuals can more efficiently and quickly produce information using VHA data.

Finally, although the VHA has several programs and services to help researchers, the ability to retrieve and use EHR and administrative data may depend on the researcher's technical knowledge and skills (e.g., knowledge of the data source structures, ability to conceptualize what data are available or can be utilized, knowledge of natural language processing or qualitative methodologies) or access to individuals with these skills.

There are several limitations to this study. The small sample size limits the ability to generalize findings to other VHA pain researchers. Because the survey relied on a convenience sample of PRWG members, this sample may not be representative of all those who use VHA EHR and administrative data for pain research. The use of nonstandardized questionnaires and tools as well as selection of data sources based on authors' pain research experience and familiarity with data sources may have affected the findings. It is possible that the survey excluded important and relevant questions and data sources.

CONCLUSIONS

As researchers continue to use VHA data for pain or other conditions, it is important to understand data sources and methods better so that protocols can be formulated to help guide future researchers and studies. Data from this survey provided an opportunity to examine VHA researchers' use of and confidence in the reliability of EHR and administrative data. We assessed respondents perception of barriers to accessing data and the adequacy of the data sources for pain research. In spite of known limitations, VHA pain researchers are capitalizing on the advantages of using EHR and administrative data to conduct pain studies to help ultimately improve healthcare services for Veterans. The VHA National Pain Management Strategy, initiated on November 12, 1998, established pain management as a national priority. Since then (and coincident with greater awareness of prescription opioid-related adverse events), pain research in VHA has increased and findings are increasingly relevant to healthcare providers and policy makers. Thus, the methods used to identify Veterans with pain need to be shared between researchers in the field, and future work comparing, contrasting, and validating these methods against patient-reported outcomes would help us to better understand the accuracy of the data used.

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Association between pain outcomes and race and opioid treatment: Retrospective cohort study of Veterans

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Abstract—We examined whether pain outcomes (pain interference, perceived pain treatment effectiveness) vary by race and then whether opioid use moderates these associations. These analyses are part of a retrospective cohort study among 3,505 black and 46,203 non-Hispanic, white Department of Veterans Affairs (VA) patients with diagnoses of chronic musculoskeletal pain who responded to the 2007 VA Survey of Healthcare Experiences of Patients (SHEP). We used electronic medical record data to identify prescriptions for pharmacologic pain treatments in the year after diagnosis (Pain Diagnosis index visit) and before the SHEP index visit (the visit that made one eligible to complete the SHEP); pain outcomes came from the SHEP. We found no significant associations between race and pain interference or perceived effectiveness of pain treatment. VA patients with opioid prescriptions between the Pain Diagnosis index visit and the SHEP index visit reported greater pain interference on the SHEP than those without opioid prescriptions during that period. Opioid prescriptions were not associated with perceived treatment effectiveness for most patients. Findings raise questions about benefits of opioids for musculoskeletal pain and point to the need for alternative treatments for addressing chronic noncancer pain.

Key words: blacks, chronic pain, Department of Veterans Affairs, disparities, opioids, pain outcomes, pain treatment effectiveness, race, survey, Veterans.

INTRODUCTION

Numerous studies have shown that blacks are less likely than whites to be prescribed opioid analgesics for a variety of pain conditions [1]. These disparities have been viewed as especially problematic in light of evidence that blacks experience chronic pain that is more severe and more disabling than whites [2–7]. Although many factors contribute to these racial disparities in pain outcomes (e.g., racial differences in patients' beliefs about pain [4,8–10], exposure to racial discrimination [11–12]), there is concern about the role of undertreatment

Abbreviations: CI = confidence interval, HSR&D = Health Services Research and Development Service, ICD-9 = International Classification of Diseases-9th Revision, NPCD = National Patient Care Database, OR = odds ratio, PTSD = posttraumatic stress disorder, SHEP = Survey of Healthcare Experiences of Patients, VA = Department of Veterans Affairs.

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of pain [1–3,13]. Consequently, recent position papers have highlighted the importance of reducing racial disparities in opioid prescription and proposed strategies to accomplish this goal [2–3].

There is a tension, however, between the imperative to address racial disparities in opioid treatment and acknowledgment of the public health crisis caused by increased prescription of opioids, particularly in light of incomplete evidence about their benefits relative to the known risks. There are limited data on the long-term effectiveness and safety of opioids for the treatment of chronic noncancer pain [14–15] and mounting evidence of serious risks associated with opioids [15–18]. Although there have been numerous studies documenting racial disparities in opioid use [1], there is scant research on whether these disparities are, in fact, associated with poorer pain outcomes for black patients.

Our prior research found that among Department of Veterans Affairs (VA) patients diagnosed with a chronic musculoskeletal condition who reported moderate or high levels of pain and who were under age 65, blacks were less likely to be prescribed opioids than their white counterparts [19]. The objectives of this study were to examine whether pain outcomes (pain interference, perceived pain treatment effectiveness) among those who reported being treated for chronic pain at VA vary by race and then whether receipt of opioid prescriptions moderates these relationships.

METHODS

Study Design

This was a retrospective cohort study using survey data from the 2007 VA Survey of Healthcare Experiences of Patients (SHEP) ambulatory care module and data extracted from the VA National Patient Care Database (NPCD). This study was approved by the institutional review board of the Minneapolis VA Health Care System.

Setting and Participants

We identified a retrospective cohort using the 2007 SHEP ambulatory care module, a national survey administered quarterly by the VA Office of Quality and Performance, to solicit patient-reported information concerning recent specific episodes of outpatient care. Each individual selected was surveyed about an episode of care (referred to as the SHEP index visit). This survey was mailed to patients early in the second calendar month following their SHEP index visit, and data collection was closed 4 wk after the survey was mailed. We identified a sample of patients with chronic pain (9,831 black and 71,471 white patients, referred to as the "chronic pain sample") using the same criteria as we used in our previous research examining racial differences in opioid prescriptions in VA [19] (**Figure 1**). The sample included non-Hispanic black or white established and new primary care patients who were selected to be in the 2007 SHEP (irrespective of whether or not they responded to the SHEP) and met the following inclusion criteria: (1) any diagnoses of back, neck, or joint pain in the year prior to the SHEP index visit; (2) no cancer diagnoses in the year prior to the SHEP index visit; and (3) no outpatient opioid prescription received in the 3 mo prior to the first pain diagnosis (Pain Diagnosis index visit). Our rationale for restricting the sample to patients who had no opioid prescription in the first 3 mo prior to the Pain Diagnosis index visit was to ensure that the opioid was prescribed for treatment of that particular pain episode rather than for a different reason. In analyses examining pain interference as an outcome, we included only those patients who responded to the SHEP (3,505 non-Hispanic blacks and 46,203 non-Hispanic whites). In our analyses examining perceived treatment effectiveness as an outcome, we further restricted our sample to those who reported on the SHEP that they were treated for chronic pain in the VA in the past year (1,622 non-Hispanic blacks and 13,758 non-Hispanic whites).

Study Outcomes

Pain interference was measured using the SHEP item: "During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?" This item is drawn from the Bodily Pain subscale of the 36-Item Short Form Health Survey (SF-36) [20]. Consistent with prior research [21–22], we dichotomized responses into two categories: (1) not at all/a little bit and (2) moderately/quite a bit/extremely. We decided to dichotomize the pain interference scale in order to capture the construct of functional limitations due to pain, in which "not at all/a little bit" represents every day aches and pains, whereas "moderately/quite a bit/extremely" represents clinically actionable pain, requiring comprehensive assessment and treatment [23].

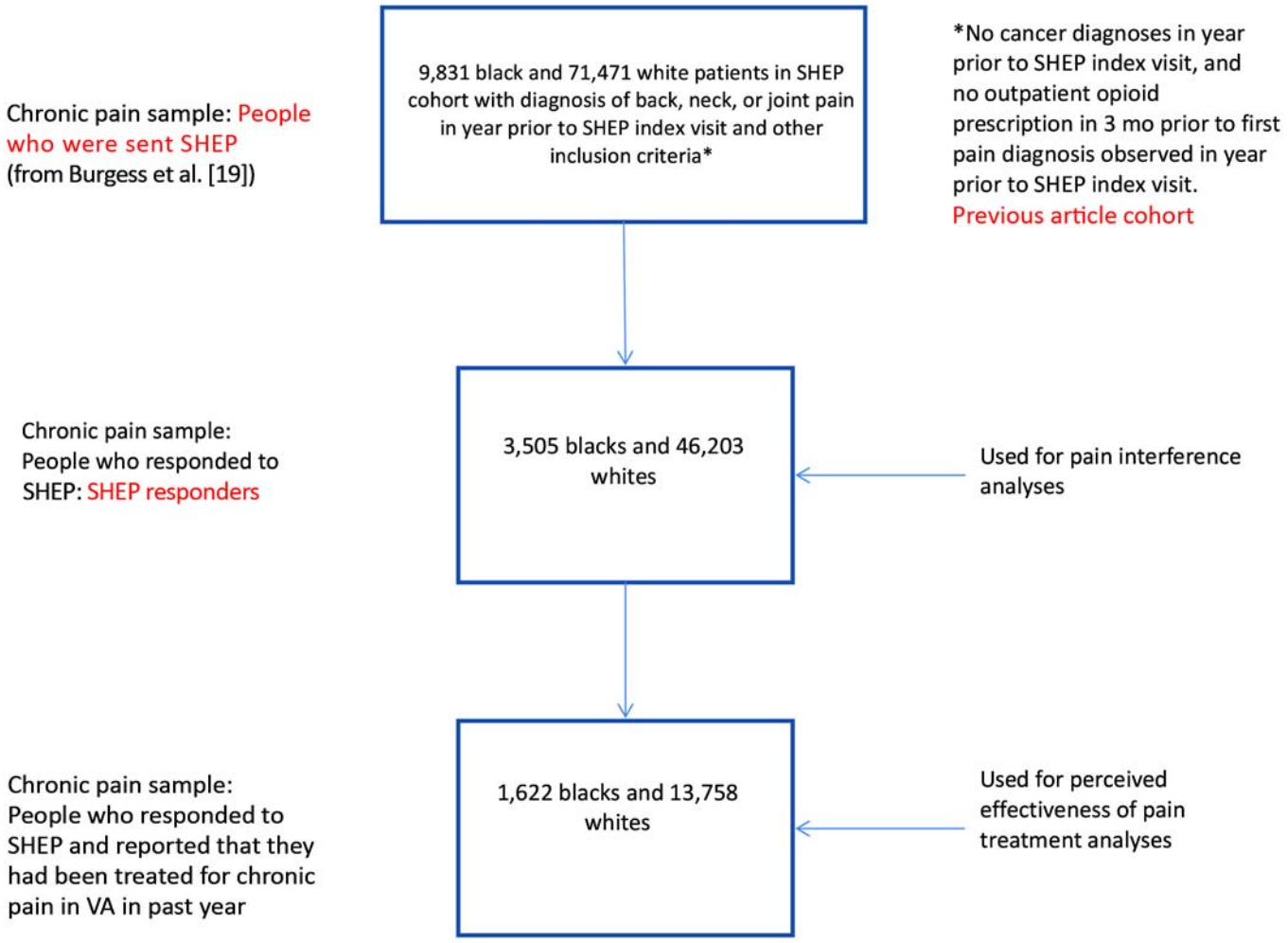

Figure 1.
Samples used to test specific hypotheses. SHEP = Survey of Healthcare Experiences of Patients, VA = Department of Veterans Affairs.

Perceived effectiveness of pain treatment among those who reported being treated for chronic pain in VA was measured using the SHEP item: "If you have been treated by a VA provider for chronic pain, please rate the effectiveness of your pain treatment." This analysis only included those patients who reported on the SHEP that they were treated for chronic pain in the VA in the past year. Response options were poor, fair, good, very good, and excellent. Previous research with Veterans has demonstrated that single-item ratings of treatment effectiveness are significantly associated with posttreatment changes in self-reported ratings of pain severity, pain interference, and disability [24]. Responses were dichotomized into two categories: (1) poor and fair and (2) good, very good, and excellent. Consistent with prior research examining differences in perceived quality of care [25], we dichotomized the perceived effectiveness scale into "poor" and "fair" versus "good," "very good," and "excellent" in order to capture whether patients perceived their chronic pain treatment as ineffective versus effective.

Primary Predictors

Patient race was obtained from the SHEP (i.e., survey self-report) and supplemented with administrative data from the NPCD when missing. The SHEP race and ethnicity measures were used to derive two categories: non-Hispanic white and non-Hispanic black.

Receipt of any opioid prescription was defined as an outpatient prescription of any opioid for any duration issued by a VA pharmacy between the Pain Diagnosis index visit and the SHEP index visit (**Figure 2**) obtained from the NPCD. The mean ± standard deviation time period between the Pain Diagnosis index visit and the SHEP index visit was 163 ± 134 d.

Demographic and Clinical Covariates

Sex and age were obtained from the NPCD. Marital status was obtained from the SHEP and supplemented with NPCD data. We used the NPCD to obtain International Classification of Diseases-9th Revision (ICD-9) diagnostic codes from outpatient visits to determine whether patients had diagnoses of medical and mental health comorbidities, including prior pain-related diagnoses (i.e., neck, back, or joint pain); opioid use disorder; or other substance use disorder during the year prior to the first pain-related diagnosis using the same codes as were used in the TROUP (Trends and Risks of Opioid Use for Pain) Study [26]. ICD-9 codes were also used to identify 30 comorbidity measures developed by Elixhauser and colleagues for use with large administrative data sets [27]. Additional diagnoses (separate from Elixhauser measures) hypothesized to be associated with pain outcomes or pain treatment: phantom limb pain, psychogenic pain, spinal cord injury, and posttraumatic stress disorder (PTSD) were included in analyses (see Burgess et al. for diagnosis codes [19]).

VA guidelines recommend screening for the presence and intensity of pain at each outpatient visit using a numerical 0 (no pain) to 10 (worst pain imaginable) rating scale. In our analysis, we used the pain intensity rating that occurred at the Pain Diagnosis index visit if it was documented in the NPCD. If there was no documented pain intensity rating at the Pain Diagnosis index visit, we used the documented pain intensity rating at the most proximal time prior to the Pain Diagnosis index visit. We categorized pain intensity ratings using standard cutpoints indicating no pain (0), mild pain intensity (ratings of 1–3), moderate pain intensity (ratings of 4–6), and severe pain intensity (ratings of 7–10) [28–29].

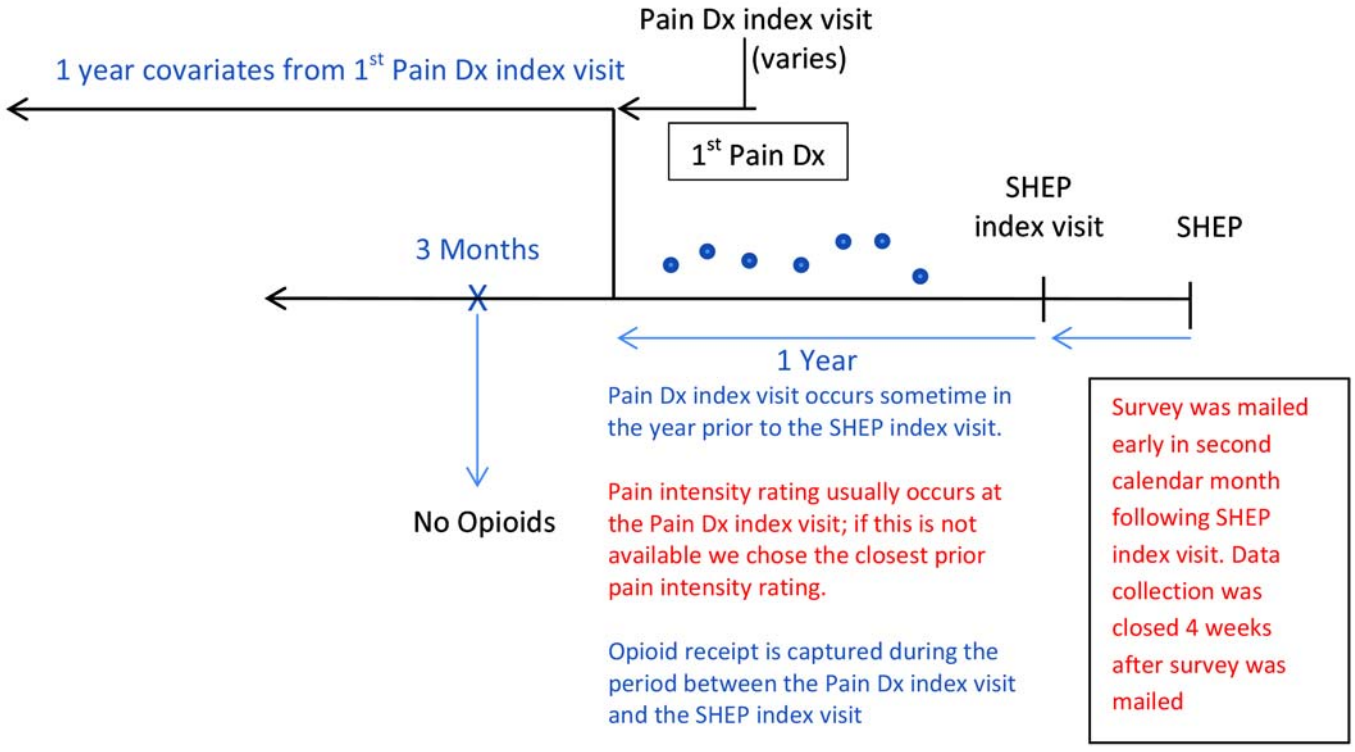

Figure 2.
Temporal structure of data. Dx = diagnosis, SHEP = Survey of Healthcare Experiences of Patients.

Healthcare utilization in the year prior to the first pain diagnosis was summarized using the number of outpatient visits and inpatient admissions from NPCD data. We obtained information about whether the patient was classified as new to primary care versus established (i.e., previous primary care visit(s)) from the SHEP, as the likelihood of receiving an opioid may be greater among established patients.

Statistical Analyses

We fit a hierarchical logistic regression model for good to excellent effectiveness of pain treatment among the members of the cohort who responded to the perceived effectiveness SHEP item and who reported being treated for chronic pain at the VA within the past year. We investigated whether race was associated with the effectiveness of treatment and, subsequently, whether opioid use moderated any association between race and treatment effectiveness. As our analyses found that the likelihood of receiving opioids varied with prior pain intensity level, we stratified these analyses by prior pain intensity ratings. Within each subgroup (no, mild, moderate, and severe pain), we fit a generalized linear mixed logistic regression model incorporating fixed effects for race (black or white), new or established primary care patient, receipt of opioids between the Pain Diagnosis index visit and the SHEP index visit, days between the Pain Diagnosis index visit and the SHEP index visit, and an interaction between race and receipt of opioids combined with the demographic, utilization, prior pain diagnoses, and comorbidity measures discussed previously. Comorbidity measures were included as covariates if there was a 5 percent or greater difference in treatment rates among those with and without the comorbidity and at least 100 members of the cohort were diagnosed with the condition. The model incorporated (Gaussian) random intercepts for each facility and (Gaussian) random race effects for each facility to allow for race differences to vary by facility and also allow us examine overall race differences through the estimated fixed effects for race. These generalized linear mixed models were implemented using pseudo-likelihood algorithms in PROC GLIMMIX, SAS, version 9.2 (SAS Institute Inc; Cary, North Carolina).

The same process was used to investigate the association between race and perceived effectiveness of chronic pain treatment and whether opioid use moderated the association between race and perceived effectiveness. We conducted this analysis among the members of the cohort who responded to the perceived effectiveness SHEP item and who reported being treated for chronic pain at the VA within the past year.

Response to the SHEP was incomplete (61% of our chronic pain sample responded to the SHEP). To assess the potential effect of survey nonresponse on the study findings, we fit a logistic regression for SHEP response using those demographic, medical and mental health comorbidities, and healthcare utilization measures that differed between responders and nonresponders as predictors. We estimated the propensity for responding to the SHEP from this model, formed eight strata from these estimated propensities, and verified that responders and nonresponders were well balanced within these strata. We then included this strata variable in the models (as an additional predictor) [30].

RESULTS

Sample Characteristics by Race

Black patients were more likely to be female and unmarried, more likely to have diagnoses of back and neck pain, and less likely to have a diagnosis of joint pain. Black patients were also more likely than white patients to have diagnoses of opioid use disorder, alcohol or drug use disorders, or a psychiatric disorder, including PTSD. (See **Table 1** for tests of statistical significance.)

Pain Interference

Pain interference was not associated with race for any level of pain intensity rating (pain intensity rating 0, $p = 0.17$; 1–3, $p = 0.54$; 4–6, $p = 0.93$; and 7–10, $p = 0.98$). Opioid use did not moderate the association between race and pain interference for any level of pain (pain intensity rating 0, $p = 0.59$; 1–3, $p = 0.41$; 4–6, $p = 0.51$; and 7–10, $p = 0.74$).

Pain interference was significantly higher for those who received an opioid prescription. The association between pain interference and opioid prescription was stronger for patients with lower pain intensity ratings: 0 (odds ratio [OR] = 1.94, 95% confidence interval [CI] = 1.71–2.19, $p < 0.001$), 1–3 (OR = 1.84, 95% CI = 1.50–2.25, $p < 0.001$), 4–6 (OR = 1.70, 95% CI = 1.42–2.04, $p < 0.001$); and 7–10 (OR = 1.45, 95% CI = 1.21–1.75, $p < 0.001$). **Table 2** presents observed and estimated prevalence ratings of pain interference for black and white patients who were and were not prescribed opioids, stratified by prior pain intensity ratings.

Table 1.
Association between patient race and demographic, health-related, and utilization characteristics. Data presented as percentage or mean ± standard deviation.

Characteristic	White (*n* = 46,203)	Black (*n* = 3,505)	*p*-Value
Established Patient (vs new)	63.47	59.86	<0.001
Demographics			
Male	95.44	90.04	<0.001
Married	68.55	48.91	<0.001
Age (yr)	68.04 ± 12.31	58.63 ± 12.80	<0.001
Physical and Mental Health			
Chronic Back Pain	26.31	30.41	<0.001
Chronic Neck Pain	4.60	5.93	<0.001
Chronic Joint Pain	77.87	74.12	<0.001
Cardiac Arrhythmias	10.08	4.48	<0.001
Chronic Heart Failure	4.28	2.82	<0.001
Chronic Pulmonary Disease	14.66	10.33	<0.001
Diabetes (uncomplicated)	21.31	23.08	0.01
Fluid and Electrolyte Disorders	1.99	2.80	0.001
Liver Disease	1.26	3.14	<0.001
Renal Failure	3.27	4.08	0.01
Sleep Apnea	3.97	4.51	0.12
Headache	2.96	5.42	<0.001
Inflammatory Bowel Disease	0.52	0.57	0.69
Neuropathy	6.35	6.62	0.53
Opioid Use Disorder	2.81	6.99	<0.001
Alcohol/Drug Use Disorder	4.34	10.13	<0.001
Depression	14.97	19.63	<0.001
Psychosis	1.32	3.05	<0.001
PTSD	5.02	9.33	<0.001
Other Mental Health Disorders	20.48	25.34	<0.001
Mean No. Outpatient Visits	16.12 ± 17.25	20.89 ± 23.82	<0.001
Mean No. Inpatient Admissions	0.05 ± 0.30	0.07 ± 0.39	<0.001

No. = number, PTSD = posttraumatic stress disorder.

Table 2.
Observed and estimated prevalence* of pain interference among black and white Veterans with and without opioid prescriptions.

Prior Pain Intensity Score	Yes Opioids						No Opioids					
	Whites			Blacks			Whites			Blacks		
	Obs *n* (%)	Est (%)	95% CI	Obs *n* (%)	Est (%)	95% CI	Obs *n* (%)	Est (%)	95% CI	Obs *n* (%)	Est (%)	95% CI
0, No Pain	1,556 (70.8)	79.8	74.6–84.2	132 (77.7)	83.3	75.2–89.2	24,184 (46.9)	67.4	60.8–73.3	1,465 (55.8)	69.6	63.1–75.4
1–3, Mild	702 (77.7)	87.2	80.0–92.2	38 (86.1)	90.9	77.0–96.7	6,352 (60.3)	79.0	68.6–86.7	387 (63.0)	78.1	67.1–86.2
4–6, Moderate	1,137 (84.0)	91.0	85.5–95.0	114 (87.4)	92.0	84.5–96.1	6,773 (72.0)	86.0	78.0–91.4	615 (73.6)	84.8	76.4–90.6
7–10, Severe	1,315 (85.5)	93.1	87.0–96.4	179 (86.9)	93.4	86.5–96.9	4,184 (78.3)	90.0	82.0–95.0	575 (82.8)	90.0	82.0–94.8

Note: degrees of freedom = 46,407.
*Calculated at typical facility with covariates (demographics, utilization, prior pain diagnoses, and comorbidities) at modal/mean values.
CI = confidence interval, Est = estimated, Obs = observed.

Perceived Effectiveness of Pain Treatment

Perceived effectiveness of pain treatment was not associated with race (pain intensity rating 0, $p = 0.24$; 1–3, $p = 0.06$; 4–6, $p = 0.37$; and 7–10, $p = 0.78$). Opioid use did not moderate the association between race and perceived effectiveness of pain treatment (pain intensity rating 0, $p = 0.71$; 4–6, $p = 0.70$; and 7–10, $p = 0.15$), except among patients with mild pain intensity ratings (1–3, $p = 0.008$); however, this is difficult to interpret because of the small cell size of black patients in this category ($n = 24$). The main effect of opioid prescription was not significant, with the exception of the mild pain intensity group (pain intensity rating 0, $p = 0.13$; 1–3, $p = 0.003$; 4–6, $p = 0.77$; and 7–10, $p = 0.37$). **Table 3** presents observed and estimated prevalence ratings of perceived effectiveness of pain treatment for black and white patients who were and were not prescribed opioids.

DISCUSSION

Among VA primary care patients with a chronic noncancer pain diagnosis, race was not associated with pain interference or with perceived treatment effectiveness. Moreover, among black and white VA patients, receipt of an opioid prescription was significantly associated with greater pain interference and was not significantly associated with perceived treatment effectiveness, except for individuals with mild pain. The results do not vary significantly by age group. Hence, our prior findings of lower rates of opioid prescriptions among blacks than whites younger than 65 yr did not appear to contribute to racial differences in pain outcomes [19].

To our knowledge, this is the only study to examine associations of racial disparities in opioid prescriptions on clinically relevant pain outcomes among chronic pain patients and one of the first to examine the effectiveness of opioid therapy in a large integrated healthcare system. Understanding the effect of racial disparities in opioid prescription is particularly important in light of mounting evidence of serious risks associated with opioids [15–18], the rapid increase in opioid prescription for chronic noncancer pain over the last 10–15 yr, and the lack of evidence on the long-term effectiveness and safety of opioids for this purpose [14–15].

Our findings raise the broader question of whether efforts to address racial disparities in pain should focus on reducing disparities in opioid prescription, as has been suggested in prior policy recommendations [3]—at least in the case of patients with chronic noncancer pain. The use of race in decisions to prescribe opioids is clearly inconsistent with good medical practice and arguably constitutes racial bias. Although our results should be considered preliminary because of our retrospective cohort study design, which precludes the ability to draw causal inferences about the effect of opioid prescription on pain outcomes, the high levels of pain interference among the majority of black and white patients with prior opioid prescriptions suggests that additional treatment modalities may be needed for patients with chronic noncancer pain. Indeed, there is growing consensus that chronic noncancer pain is best addressed by a biopsychosocial approach that acknowledges the role of psychological and environmental factors in pain [31], some of which differ by race and hence contribute to worse pain among blacks. For example, blacks experience greater pain-related fear and lower self-efficacy in coping with pain [4,8–10]. Blacks are more likely to reside in neighborhoods that make engaging in physical activity difficult [32–33]. Blacks are also more likely to be exposed to

Table 3.
Observed and estimated prevalence* of perceived effectiveness of pain treatment among black and white Veterans with and without opioid prescriptions who reported being treated at Department of Veterans Affairs for chronic pain.

Pain Intensity	Yes Opioids						No Opioids					
	Whites			Blacks			Whites			Blacks		
	Obs *n* (%)	Est (%)	95% CI	Obs *n* (%)	Est (%)	95% CI	Obs *n* (%)	Est (%)	95% CI	Obs *n* (%)	Est (%)	95% CI
0, No Pain	850 (62.7)	56.7	43.3–69.2	89 (58.1)	53.9	38.0–69.0	4,396 (66.5)	60.0	46.4–72.1	488 (59.1)	54.8	41.6–67.3
1–3, Mild	439 (67.5)	52.8	33.1–71.6	24 (37.5)	26.5	10.6–52.3	1,850 (62.4)	41.1	23.2–61.6	161 (61.4)	45.2	26.1–65.7
4–6, Moderate	764 (55.9)	62.4	47.1–75.6	82 (58.4)	66.8	49.2–80.7	2,637 (56.4)	62.1	46.3–75.6	316 (54.7)	63.9	48.3–77.0
7–10, Severe	917 (52.4)	46.0	30.3–62.5	126 (56.5)	51.3	33.9–68.4	1,905 (53.2)	45.2	29.1–62.4	336 (47.9)	42.0	26.6–58.6

Note: degrees of freedom = 15,307.
*Calculated at typical facility with covariates (demographics, utilization, prior pain diagnoses, and comorbidities) at modal/mean values.
CI = confidence interval, Est = estimated, Obs = observed.

discrimination, which has been shown to contribute to a more severe pain experience [11].

It is notable that black and white patients did not significantly differ in their perceptions of chronic pain treatment effectiveness or in their reported pain interference in our adjusted analyses. At first glance, these results seem inconsistent with the large body of literature documenting racial disparities in pain care and treatment [2,4]. However, most of the literature describing racial disparities in treatment (including several studies conducted at the VA prior to the present study [20,34–37]) examines specific types of treatment (e.g., opioid therapy, pain-relieving surgical procedures) rather than patients' evaluations of their overall quality of pain treatment. An exception is Dobscha et al. who, using data from the 2005 SHEP, found that black men perceived their pain treatment to be less effective than white men, after controlling for demographics, pain, and mental health comorbidities [20]. It is unclear whether discrepancy between the present findings and those of Dobscha et al. are due to methodological differences between the two studies or the fact that our study used data collected at a later time point, in which pain care quality in VA could have conceivably improved.

There are a number of limitations to this study and remaining questions that require additional research to address. Because we examined only VA outpatients, these results may not generalize to patients in other healthcare systems that have fewer processes and structures to support effective pain management. In addition, many improvements in pain management were implemented subsequent to when these data were collected in 2007. We also used self-reported measures of pain outcomes, which consisted of two single-item survey questions. It should be noted that the use of subjective measures of pain outcomes is consistent with standards of pain treatment, which emphasize the subjective nature of pain and stress the importance of the patient's experience of whether his or her pain is adequately relieved [13]. There is consensus that patients' satisfaction with care is an important measure of healthcare quality, and evidence that patient satisfaction is associated with important outcomes such as health status, health-related quality of life, and medication adherence [38–40]. However, future studies should use more comprehensive measures of pain outcomes, such as those recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) [29]. A related limitation is our use of a single pain intensity score to stratify the sample rather than use of multiple pain scores or a multidimensional measure of pain. Another potential limitation is that we restricted our sample to patients who did not have an opioid prescription during the 3 mo prior to their Pain Diagnosis index visit. We made this decision to ensure that the opioid prescription was for treatment of that particular chronic pain episode rather than for some other indication. Nonetheless, it is possible that this requirement (that people with pain have an opioid-free period) could limit the generalizability of these conclusions. Additionally, because our definition of opioid use included all patients who received opioid prescriptions any time during the period between the Pain Diagnosis index visit and the SHEP index visit, regardless of duration of prescription or indication, some patients might not have been taking an opioid at the time they had their pain intensity assessed. As a result, our conclusions should be interpreted with caution.

It is also unclear why the association between pain interference and opioid use was stronger among patients with lower pain intensity ratings. While opioids may reduce pain, there is also evidence that they can impair function [15,41]. It is possible that patients with lower pain intensity on opioids experienced greater pain relief at the cost of poorer functioning. Another possible explanation is that opioids may have analgesic benefits without improving functioning or reducing pain interference. This might be particularly true for patients who received opioids short-term for acute pain or for temporary exacerbations of chronic pain (i.e., "pain flares") without improving their overall perceptions of functioning or pain interference at the time the SHEP was completed. Future research is required to address this question, which cannot be answered by our study design, as it precludes the ability to draw causal inferences about the effect of opioid prescription on pain outcomes. Patients who received opioids may also have had worse disease severity or prognosis, and this underlying disease rather than opioids (or in conjunction with the opioids) may be contributing to the outcomes assessed. We also are not certain why perceived effectiveness was lower among individuals with mild chronic pain than those with moderate pain. It is possible that pain may be less of a clinical concern among those with lower levels of pain and, therefore, may not be addressed as much by their providers. Consequently, such patients may perceive their pain care to be less effective relative to those with greater

pain, whose providers may be doing more to address their pain. Future research is needed to address this novel finding. We are also unsure why so many patients received pain intensity ratings of 0 at the clinic visit in which they were given a pain diagnosis. One possibility is that patients were not asked about their pain, but the healthcare professional entered a 0 anyway. Other possibilities are that some disorders that might be presumed to be painful may not be persistently painful (e.g., osteoarthritis) or that pain may be absent when the patient is asked while seated comfortably when other vitals are being taken (e.g., in the case of low back pain or other degenerative disorders).

Several implications for research, policy, and practice flow from this work. First, randomized controlled trials that include a sufficient number of black patients are clearly needed to fill literature gaps about the appropriateness of opioids for chronic noncancer pain. Moreover, the high prevalence of black and white patients who reported substantial pain interference and who perceived their pain treatment as ineffective points to the need to improve the quality of chronic pain treatment available in primary care, where the majority of pain treatment in the VA (and the United States) occurs. Unfortunately, studies conducted in various settings, including the VA, have shown that primary care providers find chronic pain patients to be frustrating and difficult to treat and do not feel adequately prepared to provide care for them [42–43]. The growing movement toward "patient-centered medical homes," which are based on principles of accessibility, continuity, and care coordination, provides an opportunity for more effective and equitable chronic pain care [3,44]. However, because these models center on the role of primary care providers, it is critical that these providers have training in chronic pain treatment overall and in providing equitable care [3]. Such training should also ensure that providers are aware of nonopioid-based treatments for chronic pain and be familiar with the biopsychosocial model of chronic pain that acknowledges the role of psychological and environmental factors in pain [45]. One promising approach is the VA's Stepped Care Model of Pain Management, in which pain is managed by primary care providers, with support from mental health and specialty services as needed, and which is explicitly designed to promote equitable access to care [46]. A recent evaluation of this program has documented a reduction in referrals to pain medicine specialists, signifying primary care providers' greater confidence in treating chronic pain, as well as a reduction in the proportion of patients receiving high-dose opioids and an increase in referrals to physical therapy and chiropractic care [47]. Although more research is needed, this program and other collaborative care approaches to pain management [48] point to the utility of this approach for improving the quality and equity of treatment for chronic pain.

CONCLUSIONS

In our retrospective cohort study examining VA primary care patients with a chronic noncancer pain diagnosis, receipt of an opioid prescription was associated with greater pain interference and was not associated with perceived treatment effectiveness for most patients. Findings raise questions about benefits of opioids for musculoskeletal pain and point to the need for alternative treatments for addressing chronic noncancer pain.

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Correlates of prescription opioid therapy in Veterans with chronic pain and history of substance use disorder

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Abstract—Patients with a history of substance use disorder (SUD) are more likely to be prescribed opioid medications for chronic pain than patients without an SUD history; however, little is known about prescription opioid therapy in populations composed exclusively of patients with SUD. This study examined correlates of prescription opioid therapy in 214 Veterans with chronic noncancer pain and an SUD history. Participants completed psychosocial questionnaires and participated in a structured mental health diagnostic interview, and medical diagnoses and opioid pharmacy data were abstracted from their Department of Veterans Affairs electronic medical records. Participants were categorized into three groups based on opioid prescriptions in the past 90 d: no opioid therapy (n = 134), short-term (<90 d) opioid therapy (n = 31), or long-term (>/= 90 d) opioid therapy (n = 49). Relative to participants prescribed no or short-term opioid therapy, participants who were prescribed long-term opioid therapy had a greater number of pain diagnoses; reported higher levels of pain severity, interference, and catastrophizing; and endorsed lower chronic pain self-efficacy. In a multivariate model, number of pain diagnoses and pain interference were associated with a greater likelihood of being prescribed long-term opioid therapy after controlling for demographic and clinical characteristics. Findings highlight the poor pain-related functioning in patients with SUD histories who are prescribed long-term opioid therapy.

Key words: chronic noncancer pain, chronic pain, long-term opioid therapy, opioids, pain, pain interference, prescription opioid therapy, short-term opioid therapy, substance use disorder, Veterans.

INTRODUCTION

More than half of Department of Veterans Affairs (VA) primary care patients report pain, with many reporting chronic pain [1–3]. Relative to patients without chronic pain, patients with chronic pain have increased medical utilization, disability, and lost work productivity and decreased quality of life [1,4–5]. High rates of past and current alcohol and other substance use disorders (SUDs) have also been observed in patients with chronic pain [6–7].

Abbreviations: ANOVA = analysis of variance, BDI-II = Beck Depression Inventory-Second Edition, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition, LOT = long-term opioid therapy, MPI = West Haven-Yale Multidimensional Pain Inventory, NIH = National Institutes of Health, NOT = no opioid therapy, PTSD = posttraumatic stress disorder, SD = standard deviation, SOT = short-term opioid therapy, SUD = substance use disorder, VA = Department of Veterans Affairs.

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Prescription opioid therapy is commonly used to treat chronic pain in both Veteran and non-Veteran patients [8–10]. However, controversy surrounds this practice because recent studies indicate that fewer than half of patients prescribed opioids will experience a clinically significant reduction in pain intensity in the short term, with little improvement in physical function long-term [11–12]. Treating chronic pain with opioid therapy in patients with comorbid SUD may be especially difficult. Persons with chronic pain and SUD histories prescribed opioid therapy are at increased risk of opioid misuse, abuse, and diversion [2,13] as well as opioid overdose and opioid-related death [14–15]. These data have contributed to further controversy over the prescription of opioids to persons with SUD [16–18].

Several studies have identified specific patient demographic and clinical characteristics associated with prescription short-term opioid therapy (SOT) and long-term opioid therapy (LOT) among diverse samples of Veterans with and without SUD histories. These include younger age, male sex, white race, mental health diagnoses (e.g., depressive disorders and posttraumatic stress disorder [PTSD]), specific pain diagnoses (e.g., low back pain, neck or joint pain, arthritis), and greater perceived pain intensity [8–9,19–20]. Notably, Veterans with comorbid chronic pain and SUD, relative to Veterans with chronic pain and no SUD, are also more likely to be prescribed SOT and LOT at high doses [2,8,13,21–22]. No studies, however, have identified correlates of prescription opioid therapy within samples composed exclusively of patients with lifetime SUD histories, and it is unclear whether correlates of opioid therapy identified in previous studies that recruited heterogeneous patient samples will extend to SUD populations. Furthermore, previous studies that examined correlates of prescription opioid therapy have predominantly used administrative data, limiting available data to what were included in and could be extracted from patients' medical records (e.g., demographic characteristics, medical diagnoses).

The current study examined correlates of prescription opioid therapy in VA patients with chronic pain and lifetime SUD histories using data available in patients' medical records integrated with well-validated measures of psychopathology, substance use, and pain-related variables obtained through self-report questionnaires and clinical interviews. Based on prior research, we hypothesized that patients with more severe depressive and PTSD-related symptoms, an active SUD, and poor pain-related coping and functioning would be more likely to be prescribed LOT to manage pain. We further hypothesized that these relationships would remain significant even after controlling for demographic characteristics that have been associated with prescription opioid therapy in previous studies.

METHODS

Participants and Procedures

Participants consisted of a sample from a larger study at a single VA medical center in the Pacific Northwest that examined the relationship between chronic pain, hepatitis C virus infection, and substance abuse [23]. Participants were recruited by posted advertisements in the medical center, letters sent to patients with scheduled primary care appointments, announcements in mental health classes, and referral by clinicians in the medical center's Hepatology Clinic. Participants completed a single research appointment consisting of a clinical interview and completion of self-administered questionnaires. They received a $30 store gift card as compensation.

Eligible participants met the following study inclusion criteria: history of being tested for hepatitis C regardless of the result of the test (62% of enrolled participants were hepatitis C positive), age 18 yr or older, and English literacy. Patients with hepatitis C have high rates of chronic pain [24–25] and SUD [26], making this sample ideal for examining prescription opioid therapy in patients with both chronic pain and SUD histories. A total of 375 patients were screened for study eligibility, and 284 participants enrolled in the larger study between March 2009 and August 2011. Reasons for study exclusion included age greater than 70 yr (n = 1), pending litigation or disability compensation for pain (n = 28), presence of advanced liver disease (n = 50), current suicidal ideation (n = 2), current untreated psychotic-spectrum disorder (e.g., schizophrenia) or bipolar disorder (n = 2), cognitive impairment that precluded participation (n = 2), being a non-Veteran (n = 3), and incomplete responses to eligibility screening questions (n = 3).

Data Collection

Demographic Characteristics

Self-administered questionnaires assessed participant demographic characteristics, including age, sex, race, marital status, years of education, and annual income.

Pain Measures

Participants completed several well-validated and commonly used pain measures. Participants' perception of pain severity and the extent to which pain interferes with their lives was assessed with the West Haven-Yale Multidimensional Pain Inventory (MPI) severity scale (3 items) and interference scale (11 items) [27]. Pain severity and interference are widely used measures in studies of pain and have been recommended through expert consensus as core outcome measures in pain clinical trials [28]. MPI severity and interference scores range from 0 to 6, with scores lower than 2 indicating no or mild pain severity or interference, scores between 2 and 4 indicating moderate pain severity or interference, and scores higher than 4 representing severe pain severity or interference [29]. Pain-related catastrophizing was assessed with the 13-item Pain Catastrophizing Scale [30]. The Pain Catastrophizing Scale includes items that assess exaggerated negative orientation toward pain. Self-efficacy for managing pain was assessed with the 22-item Chronic Pain Self-Efficacy Scale [31], which measures individuals' beliefs about the extent to which they can manage their pain. Items on all pain measures used in the current study use numeric rating scales, and items are summed or averaged within scales to produce scale scores.

Mental Health Functioning

The 21-item Beck Depression Inventory-Second Edition (BDI-II) [32] assessed depressive symptom severity in the past 2 wk. The PTSD Checklist-Civilian Version [33] is commonly used in VA studies that examine symptoms of PTSD and evaluates the extent to which respondents experienced each of 17 PTSD-related symptoms in the past 1 mo. We chose to use the civilian rather than military version of the PTSD Checklist in order to assess current symptoms associated with "stressful life experiences." Prior research has demonstrated good psychometric characteristics of the PTSD Checklist-Civilian Version among Veterans [34–35]. For the current study, participants were classified as meeting criteria for PTSD if they responded affirmatively to an index trauma question and scored at least 50 on the PTSD Checklist. Scores above this cutoff are indicative of clinically significant PTSD symptoms [36].

Substance Use Disorders

To obtain detailed SUD histories, trained interviewers administered the SUD module of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) [37], which has demonstrated excellent psychometric properties [38]. This interview identifies patients' lifetime histories of alcohol and non-alcohol substance abuse and dependence that are consistent with DSM-IV diagnostic criteria. The Structured Clinical Interview was modified for the current study to allow for separate diagnoses of prescription opioid use disorder and illicit (e.g., heroin) opioid use disorder. Consistent with DSM-IV diagnostic criteria, participants who met criteria in the prior month for substance abuse or dependence were coded as having an active SUD. Participants who previously met criteria for substance abuse or dependence, but not in the past month, were coded as having a lifetime SUD history. For participants who met diagnostic criteria for a lifetime SUD history, we did not distinguish between those in early versus sustained remission or partial versus full remission. We used these definitions of active and lifetime SUD history to align with DSM-IV diagnostic criteria and because a purpose of the parent study was to identify the proportion of patients with current SUD symptoms that required clinical attention.

Pain Diagnoses and Opioid Prescriptions

Pain diagnoses and opioid pharmacy data were extracted from patients' electronic medical records using the Veterans Integrated Service Network-20 Data Warehouse. The Data Warehouse contains extracts of data from clinical records of regional VA facilities and national VA databases. Diagnostic data were obtained using International Classification of Diseases, 9th Edition, Clinical Modification codes listed in medical encounter data for the 5 yr preceding study assessment. Pain diagnoses included neck or joint pain, low back pain, arthritis, migraine headache, neuropathy, and fibromyalgia. Electronic medical record data also identified participants who had current opioid prescriptions from this medical center. Opioid type included codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, and propoxyphene. Notably, no participants were prescribed methadone as part of an opioid substitution program. We abstracted data on opioid type and duration in the past 90 d. Type of opioid prescribed was categorized into short-acting only (codeine, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone, and propoxyphene), long-acting only (fentanyl, methadone, and sustained-release hydromorphone, morphine, oxycodone, and oxymorphone), or concurrent short- and long-acting [39–40].

Statistical Analyses

This study included a subset of 214 participants from the larger sample who had one or more chronic pain diagnoses in the electronic medical record and met criteria for one or more active or lifetime SUDs based on the structured diagnostic interview. To identify correlates of prescription opioid therapy, we categorized participants into three groups: (1) no opioid therapy (NOT) in the past 90 d (n = 134), (2) SOT (<90 d duration; n = 31), or (3) LOT (≥90 d duration; n = 49). Similar definitions of SOT and LOT have been used in prior studies [8,20,41–42].

We conducted bivariate analyses using analysis of variance (ANOVA) for continuous variables and chi-square tests of association for categorical variables to compare demographic characteristics, mental health functioning, pain variables, and SUD diagnoses between the three opioid therapy groups. Significant omnibus ANOVA tests were followed with Fisher least significant difference pairwise comparisons. We also compared type of prescribed opioid between those on SOT versus LOT using chi-square tests of association. We next conducted a hierarchical multinomial logistic regression analysis to identify clinical and pain-related variables most strongly associated with NOT versus SOT versus LOT in the past 90 d. The goal of this analysis was to test the hypothesized correlates of prescription opioid therapy. The first step of this model controlled for demographic characteristics that have demonstrated associations with receipt of prescription opioid therapy in prior studies (age, sex, race) [8–9,19]. In the second step, we included depression symptom severity, PTSD diagnosis, and active SUD diagnosis. Data screening procedures identified high intercorrelations between five pain variables: number of pain diagnoses, pain severity, pain interference, pain catastrophizing, and chronic pain self-efficacy (see **Table 1** for variable correlations). We thus performed a backward stepwise elimination procedure for the pain variables in the third step of the model, retaining variables in the model that were significant at the $p < 0.10$ level. We chose this cutoff criterion to ensure retention of pain variables most strongly correlated with prescription opioid therapy while maintaining model parsimony [43]. All analyses employed two-tailed tests of significance.

RESULTS

This sample of 214 Veteran patients with chronic pain and SUD histories was composed predominantly of white (76%) male (94%) individuals. Of the participants, 60 percent had annual incomes less than $15,000 and 78 percent had a high school education or greater. Nearly all participants (95%) met diagnostic criteria for a lifetime alcohol use disorder, and many also met criteria for a lifetime cannabis use disorder (64%), lifetime cocaine use disorder (59%), and lifetime stimulant use disorder (54%). Thirty-nine percent of participants met criteria for a lifetime opioid use disorder and of these, 61 percent (n = 51) reported prior abuse of prescription opioids. Seventeen percent of participants (n = 36) met criteria for

Table 1.
Bivariate correlations between demographic, clinical, and pain variables.

Covariate	1	2	3	4	5	6	7	8	9	10	11
Demographic											
Age	1.00	—	—	—	—	—	—	—	—	—	—
Sex (Male = 0, Female = 1)	–0.11	1.00	—	—	—	—	—	—	—	—	—
Race (Minority = 0, White = 1)	–0.05	–0.03	1.00	—	—	—	—	—	—	—	—
Clinical											
BDI-II Depression Severity	–0.11	0.04	0.04	1.00	—	—	—	—	—	—	—
PTSD Diagnosis (No = 0, Yes, = 1)	–0.07	–0.02	0.05	0.51*	1.00	—	—	—	—	—	—
Active SUD Diagnosis (No = 0, Yes = 1)	–0.07	–0.07	–0.07	0.14†	0.18*	1.00	—	—	—	—	—
Pain											
No. of Pain Diagnoses	0.15†	–0.03	0.01	0.19*	0.11	–0.07	1.00	—	—	—	—
Pain Severity	0.13	0.05	–0.03	0.32*	0.21*	0.06	0.33*	1.00	—	—	—
Pain Interference	0.15†	–0.01	–0.01	0.43*	0.33*	0.08	0.32*	0.81*	1.00	—	—
Pain Catastrophizing	–0.05	–0.01	0.08	0.57*	0.37*	0.16†	0.24*	0.63*	0.66*	1.00	—
Chronic Pain Self-Efficacy	–0.12	–0.01	0.04	–0.35*	–0.12	–0.08	–0.25*	–0.48*	–0.56*	–0.53*	1.00

*$p < 0.01$.
†$p < 0.05$.
BDI-II = Beck Depression Inventory-Second Edition, No. = number, PTSD = posttraumatic stress disorder, SUD = substance use disorder.

an active SUD; the most common active SUD diagnoses included alcohol (64%, $n = 23$) and cannabis (22%, $n = 8$) use disorders. Only 17 percent ($n = 6$) of participants with an active SUD met diagnostic criteria for an opioid use disorder; half of these participants ($n = 3$) met criteria for illicit opioid use disorder, while the other half ($n = 3$) met criteria for prescription opioid use disorder. Nineteen participants (9%) were receiving specialty SUD treatment at the time of study assessment.

The most common pain syndromes in the sample were neck or joint pain (82%), low back pain (66%), and arthritis (57%). Having multiple pain syndromes was the norm rather than the exception; 74 percent of participants had at least two chronic pain diagnoses, with a mean ± standard deviation (SD) of 2.5 ± 1.3 pain diagnoses in the entire sample. Thirty-seven percent of participants ($n = 80$) were prescribed opioid therapy in the past 90 d, with 61 percent of those ($n = 49$) prescribed LOT. Among participants prescribed opioids, 85 percent were prescribed short-acting opioids only, 6 percent were prescribed long-acting opioids only, and 9 percent were prescribed both short- and long-acting opioids. The most commonly prescribed opioids were hydrocodone (65% prescribed SOT and 61% prescribed LOT) and oxycodone (26% prescribed SOT and 43% prescribed LOT). The mean ± SD BDI-II score in the sample was 17.1 ± 12.5, with 47 percent scoring above 17, which is representative of clinically significant depressive symptoms [32]. Of the participants, 114 (53%) were prescribed antidepressant medication at the time of study assessment. Thirty-two percent met criteria for PTSD based on PTSD Checklist scores.

Bivariate Correlates of Prescription Opioid Therapy

Table 2 provides data comparing participants in the three groups (NOT, SOT, and LOT) on demographic characteristics, mental health variables, SUD variables, pain-related variables, and type of opioid therapy received. Difference trends in depression, receipt of antidepressant medication, and PTSD were observed across the three groups, suggesting increasing depressive symptom severity and PTSD prevalence and receipt of antidepressant medication for participants prescribed opioid therapy, particularly LOT; however, these results did not reach statistical significance. Participants prescribed LOT reported poorer pain-related function and had more pain diagnoses. Specifically, participants prescribed LOT, relative to those prescribed NOT or SOT, reported greater pain severity, pain interference, pain catastrophizing, and lower self-efficacy to manage pain. Pain severity and interference were also higher in participants prescribed SOT relative to those prescribed NOT. Participants prescribed LOT had more pain diagnoses relative to those prescribed NOT or SOT. No differences in demographic or SUD variables were observed between participants prescribed NOT, SOT, or LOT.

Notably, among the 80 participants prescribed opioid therapy in the past 90 d, those prescribed LOT were less likely than those prescribed SOT to be prescribed short-acting opioids only (78% vs 97%, $p = 0.05$). However, only 22 percent of participants prescribed LOT were prescribed long-acting opioids.

Multivariate Model of Any Prescription Opioid Therapy

A multivariate hierarchical multinomial logistic regression model identified correlates of NOT ($n = 134$) versus SOT ($n = 31$) versus LOT ($n = 49$). This model controlled for age, sex, and race in the first model step. The overall step was nonsignificant (step 1 $\chi^2(6) = 2.06$, $p = 0.91$), as were each of the individual demographic covariates. The second model step, which included depressive symptom severity, PTSD diagnosis, and active SUD diagnosis, was also nonsignificant (step 2 $\chi^2(6) = 9.39$, $p = 0.15$), as were each of the mental health and SUD covariates. Candidate pain variables included in the stepwise elimination procedure in the final model step included number of pain diagnoses, pain severity, pain interference, pain catastrophizing, and chronic pain self-efficacy. The overall model step was significant (step 3 $\chi^2(4) = 37.98$, $p < 0.001$). Only number of pain diagnoses ($\chi^2(2) = 7.78$, $p = 0.02$) and pain interference ($\chi^2(2) = 24.83$, $p < 0.001$) were retained in the final model. Specifically, an increased number of pain diagnoses and greater pain interference were associated with a greater likelihood of being prescribed LOT versus NOT or SOT. Number of pain diagnoses and pain interference were unrelated to the likelihood of being prescribed SOT versus NOT. **Table 3** lists final model statistics.

DISCUSSION

This study examined correlates of prescription opioid therapy for chronic pain in a sample composed entirely of patients with lifetime SUD histories. More than one-third

Table 2.
Comparison of demographic and clinical characteristics based on receipt of opioid therapy. Data presented as mean ± standard deviation or frequency (%).

Characteristic	No Opioid Therapy (*n* = 134)	Short-Term Opioid Therapy (*n* = 31)	Long-Term Opioid Therapy (*n* = 49)	*p*-Value
Demographic				
Age (yr)	54.8 ± 8.2	54.2 ± 6.0	55.3 ± 6.4	0.82
Male	128 (95.5)	29 (93.5)	44 (89.8)	0.48
White	103 (76.9)	24 (77.4)	36 (73.5)	0.90
Marital Status				0.75
Single	30 (22.4)	6 (19.4)	13 (26.5)	
Married	28 (20.9)	8 (25.8)	12 (24.5)	
Divorced/Separated	71 (53.0)	15 (48.4)	20 (40.8)	
Widowed	5 (3.7)	2 (6.5)	4 (8.2)	
High School Education or Less	28 (20.9)	8 (25.8)	11 (22.4)	0.82
Annual Income <$15,000	79 (59.0)	22 (71.0)	28 (57.1)	0.40
Mental Health				
BDI-II	15.9 ± 12.4	17.0 ± 10.6	20.6 ± 13.6	0.08
Prescribed Antidepressant Medication	65 (48.5)	16 (51.6)	33 (67.3)	0.08
PTSD Diagnosis	34 (25.4)	13 (41.2)	21 (43.9)	0.06
SUD				
Lifetime SUD Diagnoses				
Alcohol	127 (94.8)	30 (96.8)	47 (95.9)	0.87
Cannabis	85 (63.4)	21 (67.7)	30 (61.2)	0.84
Cocaine	81 (60.4)	21 (67.7)	25 (51.0)	0.36
Stimulants	72 (53.7)	19 (61.3)	24 (49.0)	0.56
Hallucinogens	45 (33.6)	11 (35.5)	14 (28.6)	0.77
Illicit Opioids	39 (29.1)	9 (29.0)	17 (34.7)	0.76
Prescribed Opioids	34 (25.4)	8 (25.8)	9 (18.4)	0.59
Sedatives	31 (23.3)	6 (19.4)	11 (22.4)	0.93
No. of Lifetime SUD Diagnoses	3.8 ± 2.0	4.0 ± 2.2	3.6 ± 1.9	0.64
Active SUD Diagnosis	19 (14.1)	7 (22.6)	10 (20.4)	0.38
Receiving Specialty SUD Care	0 (0.0)	10 (32.3)	9 (18.4)	0.16
Pain				
Pain Diagnoses				
Neck or Joint Pain	106 (79.1)[a]	23 (74.2)[a]	46 (93.9)[b]	0.04
Low Back Pain	81 (60.4)[a]	18 (58.1)[a]	42 (85.7)[b]	<0.01
Arthritis	68 (50.7)[a]	19 (61.3)[a,b]	36 (73.5)[b]	0.02
Migraine Headache	25 (18.7)	5 (16.1)	12 (24.5)	0.59
Neuropathy	13 (9.7)	4 (12.9)	5 (10.2)	0.87
Fibromyalgia	11 (8.2)[a]	1 (3.2)[a]	9 (18.4)[b]	0.05
No. of Pain Diagnoses	2.3 ± 1.2[a]	2.3 ± 1.1[a]	3.1 ± 1.2[b]	<0.01
MPI Pain Severity	2.8 ± 1.6[a]	3.4 ± 1.4[b]	4.2 ± 1.0[c]	<0.01
MPI Pain Interference	3.1 ± 1.8[a]	3.7 ± 1.4[b]	4.7 ± 1.0[c]	<0.01
Chronic Pain Self-Efficacy Scale	1,450.6 ± 429.0[a]	1,353.9 ± 350.1[a]	1,137.6 ± 347.4[b]	<0.01
Pain Catastrophizing Scale	19.7 ± 12.8[a]	22.5 ± 13.4[a]	28.7 ± 11.7[b]	<0.01
Prescribed Opioid Therapy				
Type of Opioid				0.05
Short-Acting Only	NA	30 (96.8)	38 (77.6)	
Long-Acting Only	NA	1 (3.2)	4 (8.2)	
Both Short- and Long-Acting	NA	0 (0.0)	7 (14.3)	

Note: Values with different superscript letters significantly differ at $p < 0.05$ level.
*Based on PTSD Checklist.
BDI-II = Beck Depression Inventory-Second Edition, MPI = West Haven-Yale Multidimensional Pain Inventory, NA = not applicable, No. = number, PTSD = post-traumatic stress disorder, SUD = substance use disorder.

Table 3.
Final multivariate model examining correlates of opioid therapy. Data presented as odds ratio (95% confidence interval).

Covariate	NOT* vs SOT	NOT* vs LOT	SOT* vs LOT
Step 1: Demographic			
Age	0.99 (0.93–1.04)	0.98 (0.93–1.04)	0.99 (0.93–1.06)
Sex (Male = 0, Female = 1)	1.34 (0.25–7.04)	2.91 (0.70–12.05)	2.18 (0.33–14.08)
Race (Minority = 0, White = 1)	1.09 (0.42–2.86)	0.98 (0.41–2.34)	0.90 (0.29–2.75)
Step 2: Clinical			
BDI-II Depression Severity	0.98 (0.94–1.02)	0.98 (0.94–1.01)	1.00 (0.95–1.05)
PTSD Diagnosis (No = 0, Yes = 1)	1.86 (0.72–4.83)	1.31 (0.55–3.11)	0.70 (0.23–2.12)
Active SUD Diagnosis (No = 0, Yes = 1)	1.56 (0.79–1.40)	1.59 (0.60–4.24)	1.02 (0.31–3.36)
Step 3: Pain			
No. of Pain Diagnoses	0.95 (0.72–1.26)	1.44 (1.08–1.91)†	1.51 (1.06–2.15)†
MPI Interference Scale	1.30 (0.97–1.73)	2.12 (1.50–3.00)†	1.64 (1.09–2.46)†

Note: Final model $\chi^2(16) = 49.42$, $p < 0.001$, Nagelkerke pseudo $R^2 = 0.25$.
*NOT group served as reference category versus SOT and LOT groups; SOT group served as reference category versus LOT group.
†Association significant at $p < 0.05$ level.
BDI-II = Beck Depression Inventory-Second Edition, LOT = long-term opioid therapy, MPI = West Haven-Yale Multidimensional Pain Inventory, No. = number, NOT = no opioid therapy, PTSD = posttraumatic stress disorder, SOT = short-term opioid therapy, SUD = substance use disorder.

of participants in this sample were prescribed an opioid in the past 90 d. This percentage is slightly lower than the approximately 50 percent identified in a national sample of patients with chronic pain diagnoses seen in the VA during fiscal years 2009 through 2011 [9], the same years in which this study was conducted. This observed difference may be an artifact of the intervals over which prescription opioid therapy were measured in the two studies (i.e., 90 d in the current study vs 12 mo in the national cohort) or the potentially nonrepresentative convenience sample recruited for the current study. Notably, our sample was similar in terms of age, sex, race, and recent SUD diagnoses when compared with a nationally representative sample of 10,159 Veterans with high alcohol consumption [44], indicating the composition of our sample across these variables reflects the broader population of VA patients with SUDs. Nonetheless, additional studies using representative samples are needed that describe recent opioid prescription trends and nonopioid pain treatment use specifically in patients with lifetime SUD histories.

Our bivariate finding that participants with SUD prescribed LOT reported greater pain severity than those prescribed NOT or SOT is consistent with our hypothesis and findings from prior studies of patients with chronic pain [8,20]. Unfortunately, we do not have data documenting participant pain ratings prior to the initiation of opioid therapy to determine whether pain severity reduced as a result of LOT. It is possible that high pain ratings led clinicians to initiate opioid therapy for these participants. Indeed, previous studies demonstrated that patients with SUD are highly sensitive to pain and report greater pain severity relative to those without SUD [45–47]. In one scenario, elevated pain ratings in this group of participants prescribed LOT may represent reductions in pain severity from even higher pain ratings observed prior to opioid therapy initiation, albeit to levels still greater than pain ratings endorsed by those not prescribed opioids. Alternatively, participants prescribed LOT may have experienced near alleviation of pain when first initiating opioid therapy but over time developed opioid tolerance or opioid-induced hyperalgesia related to the chronicity of opioid therapy, resulting in a rebound of pain [48–49]. Longitudinal studies are needed to describe pain trajectories for patients with SUD prescribed opioid therapy for chronic pain to inform clinicians about when to initiate, maintain, and discontinue opioid therapy for those with SUD histories. Ideally, these studies would capture pain intensity and pain-related function prior to opioid initiation, during the course of opioid therapy, and when applicable, following opioid discontinuation.

Several findings about the type of opioids prescribed to participants in the current study are notable. Hydrocodone and oxycodone, both short-acting opioids, were the most commonly prescribed opioids in the entire sample at 63 and 36 percent, respectively. Prescription rates did not differ between participants prescribed SOT or LOT. Only 22 percent of those prescribed LOT were prescribed

any long-acting opioids, and nearly two-thirds of these participants prescribed long-acting opioids were prescribed a short-acting opioid concomitantly. While a historical diagnosis of SUD by itself would not preclude a patient with chronic pain from being prescribed opioid therapy, VA/Department of Defense opioid therapy guidelines recommend use of long-acting opioids for persistent pain and prescription of any opioid therapy for chronic pain only after other nonopioid analgesic pharmacotherapies and nonpharmacologic pain treatments have insufficiently improved pain-related function [50]. Of additional concern is that oxycodone and, recently, hydrocodone are schedule II controlled substances and prescriptions of these substances are associated with increased risk of opioid overdose death [51]. VA patients with SUD histories are also 2.5 times more likely than those without SUD histories to die by prescription opioid overdose [14], indicating that two of the "riskiest" opioids are being prescribed to this already high-risk group.

A unique contribution of this study was the measurement of patient-reported pain outcomes using well-validated measures not previously included- in studies of prescription opioid therapy and the integration of these data with administrative data available in patient medical records. Notably, average pain severity and interference scores for those in the LOT category fell in the "severe" range while pain severity and interference scores for those in the NOT and SOT categories fell in the "moderate" range. Participants prescribed LOT also endorsed greater pain catastrophizing and had poorer pain coping self-efficacy skills. In our multivariate analysis, pain interference remained the most robust correlate of LOT. Many patients with chronic pain will not experience sustained alleviation of pain, despite trials of analgesic pharmacotherapy and nonpharmacologic pain treatment [52–53]. The emphasis for these patients thus becomes improved quality of life through reduced pain-related disability, improved physical function, and enhanced coping skills [54]. Multifaceted, collaborative pain care approaches that are consistent with a biopsychosocial approach to pain management are needed for patients with comorbid SUD because prescription opioid therapy may be contraindicated for some and ineffective at adequately managing pain in others [55].

Results of this study should be considered in light of its limitations. First, we examined a convenience sample of VA patients from a single VA medical center in the Pacific Northwest who had been tested for hepatitis C virus infection, and despite a similar demographic composition of patients in our sample versus nationally representative samples of VA patients with SUD [44], results may not generalize to this larger population. Second, questionnaire and clinical interview data were cross-sectional, and we obtained pain diagnoses, opioid and antidepressant prescription data, and specialty SUD treatment utilization retrospectively from participants' medical records. As such, causal inferences cannot be drawn from these data. Third, we included participants with a lifetime history of any SUD. Some substances when combined with opioids (e.g., alcohol, benzodiazepines) may confer greater risk of opioid-related adverse events than others (e.g., cannabis). Future studies should examine which SUDs, or combination of SUDs, moderate opioid prescribing practices. Fourth, participants with lifetime SUD histories included individuals in early and partial remission from an active SUD, and receipt of opioid therapy may differ between these individuals and those with SUD in full sustained remission. Fifth, we were unable to verify adherence to prescribed opioid therapy or whether participants obtained opioid prescriptions from non-VA sources. Sixth, we did not evaluate opioid therapy retrospectively beyond 90 d prior to the study assessment. As such, we were unable to assess the duration of continuous opioid therapy for those in the LOT category or determine whether participants in the NOT category had previously been prescribed opioid therapy for pain. Seventh, we did not obtain information about nonopioid pain treatment received in the 90 d prior to the study encounter. It is thus unclear what adjunctive services participants may have been using concurrently with, or as alternatives to, opioids to manage pain. Finally, sample size limitations may have contributed to our failure to obtain statistically significant findings for variables previously shown to be associated with opioid therapy (e.g., PTSD and active SUD diagnoses) [8,20].

CONCLUSIONS

In summary, we found that among a sample of VA patients with chronic pain and lifetime SUD histories, those prescribed opioid therapy, particularly LOT, had higher pain severity and poorer pain-related function and coping. Unfortunately, little is known about the effectiveness of pain treatments for patients with SUD because pain therapy clinical trials have historically excluded

these patients [56]. Additional research is needed to identify evidence-based pain treatments for patients with chronic pain and SUD that reduce pain and improve physical function while minimizing the deleterious consequences of substance misuse and abuse.

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Does comorbid chronic pain affect posttraumatic stress disorder diagnosis and treatment? Outcomes of posttraumatic stress disorder screening in Department of Veterans Affairs primary care

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Abstract—Because posttraumatic stress disorder (PTSD) is both prevalent and underrecognized, routine primary care-based screening for PTSD has been implemented across the Veterans Health Administration. PTSD is frequently complicated by the presence of comorbid chronic pain, and patients with both conditions have increased symptom severity and poorer prognosis. Our objective was to determine whether the presence of pain affects diagnosis and treatment of PTSD among Department of Veterans Affairs (VA) patients who have a positive PTSD screening test. This retrospective cohort study used clinical and administrative data from six Midwestern VA medical centers. We identified 4,244 VA primary care patients with a positive PTSD screen and compared outcomes for those with and without a coexisting pain diagnosis. Outcomes were three clinically appropriate responses to positive PTSD screening: (1) mental health visit, (2) PTSD diagnosis, and (3) new selective serotonin reuptake inhibitor (SSRI) prescription. We found that patients with coexisting pain had a lower rate of mental health visits than those without pain (hazard ratio: 0.889, 95% confidence interval: 0.821–0.962). There were no significant differences in the rate of PTSD diagnosis or new SSRI prescription between patients with and without coexisting pain.

Key words: comorbidity, health services research, healthcare utilization, mental health, pain, posttraumatic stress disorder, primary care, screening, Veterans, Veterans health.

INTRODUCTION

Posttraumatic stress disorder (PTSD) is both prevalent and underrecognized in primary care. Prior to operations in Iraq and Afghanistan, the point prevalence of PTSD among Department of Veterans Affairs (VA) primary care patients was estimated at 11.5 percent and the diagnosis was recognized by the primary care provider in less than 50 percent of cases [1]. Routine screening with the 4-item Primary Care PTSD Screen (PC-PTSD) has

Abbreviations: CI = confidence interval, ICD-9 = International Classification of Diseases-9th Revision, PC-MHI = Primary Care-Mental Health Integration, PC-PTSD = Primary Care PTSD Screen, PTSD = posttraumatic stress disorder, SSRI = selective serotonin reuptake inhibitor, VA = Department of Veterans Affairs.

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been implemented within the VA system to facilitate early recognition of PTSD [2].

PTSD is frequently complicated by the presence of comorbid chronic pain. Studies of Veterans in all eras since Vietnam have yielded high rates of comorbidity between the two conditions [3–5]. Patients with comorbid PTSD and pain have worse symptom severity, worse prognosis and treatment outcomes, greater levels of disability, worse quality of life, greater levels of psychological distress, and worse maladaptive thinking and coping patterns [6–12]. Theoretical models have postulated underlying vulnerabilities that predispose the development of both chronic pain and PTSD [13] as well as multiple ways in which the two conditions exacerbate and maintain one another [14].

Previous research has shown that co-occurrence of depression and pain is associated with a decreased likelihood that depression will be appropriately diagnosed and treated [15]. This may occur because patients or clinicians prefer to focus on managing physical symptoms [16]. Whether similar effects occur in comorbid PTSD and pain is unknown, but it is plausible given the commonalities between chronic pain and PTSD of avoidant coping style, reduced activity, and social withdrawal that may affect healthcare utilization [14]. Depression management has been the focus of considerable attention in primary care and is now principally managed by generalist providers in primary care. PTSD differs in that it has received less attention in primary care and the most effective evidence-based therapies for PTSD are typically delivered in mental health settings; however, initial diagnosis and treatment or referral usually occur in primary care. Following a positive screen and further evaluation of symptoms, current VA guidelines advise primary care providers to manage PTSD by initiating pharmacotherapy (primarily selective serotonin reuptake inhibitors [SSRIs]) and/or referring to psychotherapy [17].

Our objective was to determine whether coexisting pain affects diagnosis and treatment of PTSD among VA patients who have a positive PTSD screening test in primary care. Based on previous literature on chronic pain and comorbid depression in primary care patients [16], we hypothesized that the presence of pain would predict longer delays in PTSD evaluation and treatment outcomes following positive PTSD screenings in primary care. We evaluated time to mental health visit, time to PTSD diagnosis, and time to new SSRI prescription as our outcomes.

METHODS

This retrospective cohort study included patients receiving care within Veterans Integrated Service Network 11, the VA regional healthcare network serving Michigan, Indiana, and Illinois. Clinical and administrative data were extracted from local databases of six VA medical centers. We included patients who had a positive PTSD screening test between January 1, 2001, and January 1, 2007, and had a primary care visit within 30 days after the positive screening. We excluded patients from this analysis if they had a preexisting PTSD diagnosis (International Classification of Diseases-9th Revision [ICD-9] 309.81) or if they had no primary care visit within 30 days of the positive screening test. Outcomes that occurred up to January 1, 2008, were analyzed.

Measures

VA clinical sites included in this study used the PC-PTSD to screen for PTSD in primary care clinics. The PC-PTSD was developed and validated among Veterans seen in outpatient VA primary care clinics and implemented nationally. A score of 3 has been determined to be the optimally efficient cutoff and is used by VA as the cutoff for a positive screen [2,18]; accordingly, we considered a score of ≥3 to be a positive screen for this study. A positive screen on the PC-PTSD has a positive predictive value of 0.65 and a negative predictive value of 0.92 for clinical PTSD diagnosis [2].

The primary independent variable was coexisting pain, defined as an ICD-9 diagnostic code for a pain diagnosis in the year prior to the positive PTSD screen. We used ICD-9 codes for headache (346, 307.81, 784.0, 62.72, 339), back pain (720–724), arthritis and joint pain (710–719, 725–739.9), and nonspecific pain conditions (780.96, 307.8, 307.89, 338), which account for the vast majority of chronic pain diagnoses among Veterans [19–22]. We also used ICD-9 codes to determine the presence of depression (296.2, 296.3, 311), alcohol use disorder (303.9, 305.0), and drug use disorder (304, 305.2–305.9) in the year prior to the positive PTSD screen.

Outcomes

We examined outcomes representing potential clinical responses to positive PTSD screening. The screening outcomes examined were (1) time to mental health visit, (2) time to PTSD diagnosis, and (3) time to new SSRI prescription. Mental health visits included those to both

general mental health and substance use disorder clinics. PTSD diagnosis was defined by an ICD-9 code of 309.81. SSRI use was evaluated by review of VA outpatient pharmacy prescription dispensing data, which included medication names and dates for all prescriptions filled.

Statistical Analysis

We compared characteristics of patients with and without coexisting pain using chi-square and *t*-tests for categorical and continuous variables, respectively. Survival analyses of time from first positive PTSD screening to time of mental health visit, time of PTSD diagnosis, and time of new SSRI prescription were conducted using Kaplan-Meier estimates for determining median time to event and event rates at specific times. Analyses of time to SSRI prescriptions excluded participants with an SSRI prescription in the prior year. We then used Cox's proportional hazards regression to evaluate the association between coexisting pain and PTSD screening outcomes over time; separate Cox models were used to determine the effect of comorbid pain on each outcome. Cox proportional hazards assume hazard ratios of effects are constant over time. Each model included the following covariates: age, sex, mental health visit in the previous year, depression, alcohol disorder, drug disorder, and medical comorbidity as derived from the Romano adaptation of the Charlson index [23–24]. Interactions between site and pain were not significant, so site-specific analyses were not conducted. Analyses were conducted using SAS 9.2 (SAS Institute Inc; Cary, North Carolina).

RESULTS

After exclusion of 1,361 patients with a prior PTSD diagnosis and 479 who had no primary care visit within 30 days of PTSD screening, the cohort included 4,244 patients with a positive PTSD screen. The majority of included patients had a primary care visit the same day as their PTSD screening test (n = 4,028, 94.9%). The mean age was 50.4, and 91.9 percent of patients were male. Race data were missing on 56.1 percent of cohort members. Half of the cohort (49.6%) had a coexisting pain diagnosis, and 38.6 percent had a current analgesic prescription (**Table 1**). Patients with a pain diagnosis were slightly younger (48.8 vs 52.0 yr old, $p < 0.001$) and more often had depression (33.4% vs 29.4%, $p = 0.005$) than those without pain (**Table 2**).

Table 1.
Baseline characteristics of patients who screened positive for posttraumatic stress disorder (N = 4,244).

Characteristic	Mean ± SD or *n* (%)
Age (yr)	50.4 ± 15.9
Male	3,900 (91.9)
Race	
White	1,636 (38.5)
Black	228 (5.4)
Unknown	2,380 (56.1)
Depression Diagnosis	1,331 (31.4)
Alcohol Disorder Diagnosis	415 (9.8)
Drug Disorder Diagnosis	178 (4.2)
Mental Health Visit in Past Year	907 (21.4)
Comorbidity (Charlson Index score)	0.64 ± 1.01
Pain Diagnosis*	2,104 (49.6)
Back	971 (22.9)
Joint or Limb	1,385 (32.6)
Headache	238 (5.6)
Current Pain Medication	1,638 (38.6)
Pain Score† (≥4)	1,689 (39.8)

*Some participants recorded >1 pain location.
†Self-rated between 0 and 10 by patients.
SD = standard deviation.

Mental Health Visit

Overall, the median time to a mental health visit was 5.7 mo (95% confidence interval [CI]: 4.6–6.9 mo) and 56.4 percent had a mental health visit in the year after the positive PTSD screening result. **Table 3** shows the number of patients with a mental health visit at 3, 6, 9, and 12 mo after the positive PTSD screening test. Patients with coexisting pain had a statistically significant lower rate of mental health visits than those without pain (**Table 4**); however, this difference was small. In the multivariate model, patients with pain had a lower rate of mental health visits (HR: 0.889, 95% CI: 0.821–0.962) than those without pain.

Posttraumatic Stress Disorder Diagnosis

During the study follow-up period, 1,280 (30%) patients who had a positive PTSD screen received a PTSD diagnosis. **Table 3** shows the number of patients who received a PTSD diagnosis at 3, 6, 9, and 12 mo after the positive PTSD screening test. For those who received a PTSD diagnosis, the median time to diagnosis was 12.7 mo. Patients with and without coexisting pain did not significantly differ in PTSD diagnosis rates (HR: 0.968, 95% CI: 0.866–1.082).

Table 2.
Unadjusted comparison of patients who screened positive for posttraumatic stress disorder with and without pain. Data presented as mean ± standard deviation or *n* (%).

Characteristic	No Pain (*n* = 2,140)	Pain (*n* = 2,104)	*p*-Value*
Age (yr)	52.0 ± 15.9	48.8 ± 15.6	<0.001
Male	1,984 (92.7)	1,916 (91.1)	0.05
Depression Diagnosis	629 (29.4)	702 (33.4)	0.005
Alcohol Disorder Diagnosis	204 (9.5)	211 (10.0)	0.59
Drug Disorder Diagnosis	83 (3.9)	95 (4.5)	0.30
Mental Health Visit in Past Year	443 (20.7)	464 (22.1)	0.28
Charlson Comorbidity Index Score†			<0.001
0	1,205 (56.3)	1,361 (64.7)	
1	574 (26.8)	452 (21.5)	
≥2	361 (16.9)	291 (13.8)	

*Unadjusted comparison between those with and without pain.
†Categorized for ease of interpretation. Range = 0–8. *p*-Value is for continuous score.

Table 3.
Outcomes of screening at 3, 6, 9, and 12 mo after positive posttraumatic stress disorder (PTSD) screen, *n* (%).

Time Point (mo)	Mental Health Visit*	PTSD Diagnosis	New SSRI Prescription
3	1,842 (44.7)	929 (22.3)	667 (0.2)
6	2,063 (50.3)	1,017 (24.5)	784 (0.2)
9	2,194 (53.8)	1,074 (26.1)	875 (0.3)
12	2,283 (56.4)	1,132 (27.7)	938 (0.3)

*Kaplan-Meier survival rates.
SSRI = selective serotonin reuptake inhibitor.

Table 4.
Relationship between pain comorbidity and outcomes of screening.

Outcome	Pain vs No Pain, HR (95% CI)	*p*-Value
Mental Health Visit	0.889 (0.821–0.962)	0.004
PTSD Diagnosis	0.968 (0.866–1.082)	0.57
New SSRI Prescription	0.996 (0.885–1.122)	0.95

Note: Survival analysis adjusted for age, sex, prior mental health visit, depression, alcohol disorder, drug disorder, and Charlson comorbidity index score.
CI = confidence interval, HR = hazard ratio, PTSD = posttraumatic stress disorder, SSRI = selective serotonin reuptake inhibitor.

We subsequently examined the relationship between mental health visits and PTSD diagnosis. Patients who had a mental health visit after their positive PTSD screen were more likely than those without a mental health visit to receive a diagnosis of PTSD (HR: 1.388, 95% CI: 1.232–1.563). Among those who received a PTSD diagnosis, 780 (59.4%) were diagnosed by a mental health clinician.

Selective Serotonin Reuptake Inhibitor Prescription

Approximately 17 percent of participants (*n* = 720) had received an SSRI prescription within 12 mo preceding their PTSD screening and were thus excluded from the SSRI survival analysis. **Table 3** demonstrates the number of patients with a new SSRI prescription at 3, 6, 9, and 12 mo following the positive PTSD screen. There was no significant difference in time to SSRI prescription between the positive and negative PTSD screening groups (**Table 4**).

DISCUSSION

Contrary to our hypotheses, coexisting pain did not substantially affect follow-up of positive PTSD screening. Comorbid pain was not associated with significant

differences in time to PTSD diagnosis or time to SSRI prescription. Although patients with pain demonstrated longer times between a positive PTSD screen and a mental health visit, the difference was small.

Nearly half of the sample did not visit a mental health provider following the positive PTSD screening in primary care, 70 percent were not diagnosed with PTSD during the follow-up period, and 83 percent did not receive SSRI medication. Our results are consistent with data from previous research but show even lower rates of postscreening diagnosis and pharmacotherapy. A recent study of primary care screening outcomes demonstrated that only about half of patients with positive PTSD screens (56%) progressed to some form of treatment (either medication only, psychotherapy only, or a combination of the two) [25]. In a similar study, only 39 percent of patients attended a mental health visit and 48 percent received antidepressant medication following a positive PTSD screening test [26].

We do not know the optimal rates of these follow-up outcomes; presumably, some proportion of positive screening tests was determined by the primary care provider to represent false positives that did not require follow-up assessment or treatment outside primary care. In other cases, patient preference or barriers to mental health care may have affected outcomes. Prior literature indicates that many patients do not acknowledge their PTSD, are not aware that it can be treated, do not want treatment for it, or perceive a stigma related to seeking and receiving treatment [27–29].

A large majority of the sample was not diagnosed with PTSD following a positive screen in primary care; however, we do not know how many patients were evaluated and found not to meet diagnostic criteria for PTSD or how many patients were not evaluated at all. Previous literature examining PTSD in primary care found that providers identified and documented PTSD in only 11 percent of primary care patients with the diagnosis following positive PTSD screening [30]. In a separate study, primary care providers were more likely to label any evident distress as depression rather than the PTSD identified by research assessment instruments [31].

Although prior studies have found that comorbid pain is associated with a decreased likelihood that depression will be appropriately diagnosed and treated [13], we did not find a similar overall effect of comorbid pain on PTSD screening outcomes. This may be due to differences in the usual process of care for depression, which is most often managed in primary care, versus PTSD, which is usually managed in mental health clinics. Perhaps PTSD remains difficult to recognize and address in primary care regardless of comorbid medical conditions despite the guidance of PTSD screening tools.

The last year of this study overlapped with the 2007 start of the national implementation of the VA Primary Care-Mental Health Integration (PC-MHI) program [32]. This initiative systematically installed colocated and collaborative mental health providers within primary care clinics across VA. This program's effect on outcomes of positive PTSD screening in primary care is not yet fully known. One study demonstrated the benefit of PC-MHI with improved consult completion rates and higher PTSD diagnosis rates as compared with referrals from specialty care [33]; however, there were no differences by referral source in follow-up visits in the PTSD clinic. The current study is limited by the age of the data and therefore does not account for the ongoing efforts across VA to improve PTSD care; we cannot infer whether PTSD screening outcomes have changed since the data were collected. Future research should compare postscreening PTSD evaluation and treatment rates from before versus after the implementation of mental health programs in primary care to see what differences may emerge.

This study has additional limitations. First, as mentioned previously, we do not know the true rate of PTSD in the population and therefore are unable to evaluate appropriateness of follow-up among patients with and without pain. Second, diagnostic codes for pain are imprecise and noninformative regarding pain severity, pain control, and other pain outcomes, which is an inherent limitation of administrative data sets. Third, these administrative data did not provide the reasons for which SSRIs were prescribed; it is plausible that some patients were started on an SSRI for depression rather than PTSD. It also may be the case that mental health visits were initiated for reasons other than PTSD. Finally, although this study included diverse Midwestern VA sites, findings may not generalize to other VA and non-VA settings.

Despite its limitations, this study makes an important contribution to the literature as the first to examine the effect of comorbid pain on the diagnosis and treatment of PTSD following a positive PTSD screening test in VA primary care. A recent systematic review and report on PTSD screening in primary care indicated a need for studies "examining the impact of mental health screening on the primary care encounter within the VA system" [34,

p. 4]. Further research is warranted to explore in depth the likely multifaceted explanations behind these findings. For example, it would be important to understand whether age or era of service affects PTSD screening outcomes; newly returning Operation Iraqi Freedom/Operation Enduring Freedom/Operation New Dawn Veterans are typically younger than our sample's average age of 50.4 yr and have often been exposed to more combat experiences that are traumatic and injurious and thus may demonstrate different patterns of healthcare utilization related to symptoms of PTSD and chronic pain [35].

CONCLUSIONS

We examined outcomes of positive PTSD screening in VA primary care among Veterans with and without pain diagnoses. Patients with coexisting pain did not differ in time by PTSD diagnosis or new SSRI prescription and had longer delays to mental health visits than those without pain. Given that there are effective psychological treatments for chronic pain (i.e., cognitive behavioral therapy [36], acceptance and commitment therapy [37]) and PTSD (i.e., prolonged exposure [38], cognitive processing therapy [39]), it is crucial to ensure that Veterans living with both conditions are offered these interventions. Across the board, regardless of pain comorbidity, diagnosis and treatment rates following positive PTSD screenings were low. This gap following positive PTSD screens in primary care represents an area of potential promise for implementation strategies to identify and address the specific barriers to postscreening diagnosis and treatment.

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Study concept and design: E. E. Krebs.
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Fibromyalgia syndrome care of Iraq- and Afghanistan-deployed Veterans in Veterans Health Administration

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Abstract—Little is known regarding fibromyalgia syndrome (FMS) care among Operation Iraqi Freedom/Operation Enduring Freedom/Operation New Dawn (OIF/OEF/OND) Veterans. Current recommendations include interdisciplinary, team-based combined care approaches and limited opioid use. In this study of OIF/OEF/OND Veterans who accessed Veterans Health Administration services between 2002 and 2012, we hypothesized that combined care (defined as at least 4 primary care visits/yr with visits to mental health and/or rheumatology) versus <4 primary care visits/yr only would be associated with lower risk of at least 2 opioid prescriptions 12 mo following an FMS diagnosis. Using generalized linear models with a log-link, the Poisson family, and robust standard errors, we estimated risk ratios (RRs) and 95% confidence intervals (CIs). We found that 1% of Veterans had at least 2 FMS diagnoses (International Classification of Diseases-9th Revision-Clinical Modification code 729.1) or at least 1 FMS diagnosis by rheumatology. Veterans with (vs without) FMS were more likely to be female, older, Hispanic, and never/currently married. Combined primary, mental health, and rheumatology care was associated with at least 2 opioid prescriptions (RR [95% CI] for males 2.2 [1.1–4.4] and females 2.8 [0.4–18.6]). Also, combined care was associated with at least 2 nonopioid pain-related prescriptions, a practice supported by evidence-based clinical practice guidelines. In tandem, these results provide mixed evidence of benefit of combined care for FMS. Future studies of healthcare encounter characteristics, care coordination, and benefits for Veterans with FMS are needed.

Key words: Afghanistan, fibromyalgia syndrome, healthcare setting, healthcare utilization, Iraq, OIF/OEF/OND, opioid, primary care, PTSD, rheumatology, Veteran.

INTRODUCTION

The prevalence of fibromyalgia syndrome (FMS), a condition characterized primarily by widespread chronic musculoskeletal pain, has been estimated to range from

Abbreviations: CI = confidence interval, DOD = Department of Defense, DSS = Decision Support System, FMS = fibromyalgia syndrome, HSR&D = Health Services Research and Development Service, ICD-9-CM = International Classification of Diseases-9th Revision-Clinical Modification, OIF/OEF/OND = Operation Iraqi Freedom/Operation Enduring Freedom/Operation New Dawn, PTSD = posttraumatic stress disorder, RR = risk ratio, VA = Department of Veterans Affairs, VHA = Veterans Health Administration, VINCI = VA Informatics Computing Infrastructure.

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1.0 to 6.0 percent in the U.S. civilian population [1–2]. Among U.S. Department of Defense (DOD) healthcare beneficiaries aged <65 yr, a prevalence of 0.7 percent has been reported [3]. Females and older individuals are more likely to be diagnosed with FMS [3–5].

The prevalence and characteristics of Operation Iraqi Freedom/Operation Enduring Freedom/Operation New Dawn (OIF/OEF/OND) Veterans (both deployed and nondeployed) with FMS are unknown. There is also little research on the healthcare utilization of Veterans with FMS and possible variations in treatment across different healthcare providers and clinics within the Veterans Health Administration (VHA).

Generally, evidence-based practice guidelines recommend patient-tailored approaches that may include several nonpharmacologic and pharmacologic strategies to reduce symptoms and improve functionality [6–9]. Briefly, nonpharmacologic strategies include patient education, graded exercise, cognitive behavioral therapy, and complementary and alternative medicine therapies. Pharmacologic strategies include treatment with serotonin norepinephrine reuptake inhibitors, treatment with other nonopioid pain-related medications, and limited treatment with opioids. Guidelines also recommend interdisciplinary and integrative team-based approaches that include regular primary care visits and possible comanagement with mental health and rheumatology specialists [6–11]. Whether interdisciplinary, team-based combined care approaches are associated with best practices, e.g., less opioid use and more use of nonopioid pain-related medication, is unknown.

To support the implementation of evidence-based management of FMS in the VHA, we examined characteristics and healthcare utilization of OIF/OEF/OND Veterans with FMS. Our specific objectives were to describe sociodemographic and military characteristics of Veterans with FMS and to identify primary clinical sites of FMS diagnoses. Our secondary objective was to test the hypothesis that Veterans managed by an interdisciplinary, team-based approach of care for FMS (vs Veterans who are not) are less likely to be prescribed opioid medications and more likely to be prescribed nonopioid pain-related medications in the 12 mo following a FMS diagnosis. We defined a proxy variable for an interdisciplinary, team-based approach of care for FMS as combined utilization of regular primary care with mental health and/or rheumatology care within 12 mo of a diagnosis.

METHODS

Study Setting

Our cross-sectional study included Veterans from the national OIF/OEF/OND Roster file that is provided to the Department of Veterans Affairs (VA) Central Office Environmental Epidemiology Service by the Defense Manpower Data Center. The OIF/OEF/OND Roster includes Veterans who are a subset of military discharges identified as having VHA healthcare utilization. The OIF/OEF/OND Roster file was merged with data in the VA Informatics Computing Infrastructure (VINCI) [12]. These data include basic demographic files, clinical data, and all national inpatient and outpatient services provided to VHA healthcare users. Data for outpatient services in VHA include 6-digit Decision Support System (DSS) identifiers. These DSS identifiers are used to characterize outpatient clinic settings and are the single and critical designation by which VHA defines outpatient clinical work units for costing purposes [13]. The first 3 digits of the DSS identifier, or primary "stop code," designate the main clinical group responsible for patient care. The last 3 digits of the DSS identifier, or secondary "stop code," can be used by a VHA medical facility to further specify the main clinical group, for example, to specify the type of service provided or type of provider/team that administered the care. The list of nationally standardized codes is reviewed and updated at least annually by VHA's National Stop Code Council, and lists of stop code changes and active stop codes as well as a current stop code instructional guide are posted on the DSS Identifier Web page.

Participants

The OIF/OEF/OND Roster included 647,288 male and 90,819 female Veterans who accessed VHA from fiscal years 2002–2012. Of these, we identified 15,420 male and 4,179 female Veterans who had ≥1 outpatient diagnosis of FMS by the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM) code 729.1: myalgia and myositis, unspecified. Researchers have cautioned that a single ICD-9-CM FMS diagnosis or diagnoses in nonrheumatology settings may have limited specificity to identify true FMS cases [1,14–15]. To improve the specificity of our FMS case definition and to be consistent with prior research of VHA administrative data [16], we only included Veterans who received ≥1 FMS diagnosis in a rheumatology specialty care setting

(identified by corresponding clinic stop code of 314) or ≥2 FMS diagnoses on separate dates within 12 mo, regardless of outpatient care setting. There were 5,963 male and 2,245 female Veterans who met our FMS case definition.

Outpatient Settings of Index FMS Diagnoses

We defined the date of index FMS diagnosis to be the date of whichever came first: (1) the date of diagnosis in a rheumatology specialty care setting or (2) the first date of ≥2 FMS diagnoses (on separate dates) within 12 mo. We used the term "index FMS date" to distinguish our analysis from one that examines incident FMS, since we did not determine whether Veterans were free of FMS before the index date. In addition to rheumatology, we examined the top 10 primary stop codes where an FMS diagnosis was coded, stratified by male and female Veterans, on the date of index FMS diagnosis.

Exposure Definitions: Utilization of Primary Care and Mental Health and Rheumatology Specialty Care

We classified primary care encounters to be any VHA visits with a primary stop code of 342, 348, 350, or 323, excluding secondary stop code 135. We classified encounters by mental health to be any VHA visits with a primary stop code of 502–524, 527–599, or 725–731. Rheumatology specialty care visits were classified by any VHA visits with a primary stop code of 314. Multiple visits for categories of primary care, mental health, or rheumatology were counted only if they occurred on separate dates. Follow-up by primary care, mental health, and/or rheumatology was examined 12 mo after the index FMS date. In the absence of an explicitly stated definition of regular primary care in the current VA/DOD Clinical Practice Guideline for the Management of Chronic Multisymptom Illness [17], we used an empirically derived definition for regular primary care as greater than or equal to the median number of visits over 12 mo of follow-up from the index date of FMS diagnosis.

Outcome Definitions: Pharmacologic Outcomes

We examined the number of uniquely dated prescriptions generated for opioid and nonopioid pain-related medications during the 12 mo after the index FMS date. A complete list of opioid and nonopioid pain-related medications included in our analyses is in **Appendix 1** (available online only). We dichotomized users of opioid and nonopioid pain-related medications separately using a cutoff of ≥2 uniquely dated prescriptions in the 12 mo after the index FMS date.

Definitions of Potential Confounding Variables

Sociodemographic and Military Service Characteristics

We examined sociodemographic characteristics including age, race, marital status, and education. We reported age at date of first VHA encounter and age at index FMS date. We also examined factors related to Veterans' military service component (Active Duty vs reserve), rank, and branch of service.

Mental Health Comorbidities

Because mental health diagnoses of anxiety, posttraumatic stress disorder (PTSD), and depression have been associated with FMS and are risk factors for opioid prescriptions [18], we examined these mental health diagnoses associated with outpatient encounters during the 12 mo following the index FMS date. We used ICD-9-CM diagnostic codes 300.00–300.09, 300.20–300.29, and 300.3 to categorize anxiety; code 309.81 to categorize PTSD; and codes 296.20–296.25, 296.30–296.36, 300.4, and 311 to categorize depression diagnoses according to a previously published study of mental health diagnoses in the OIF/OEF/OND Veteran population [19]. These represent a cluster of mood and anxiety disorders that most prior FMS research has focused on [20–21], but it is not an exhaustive list. Others include conversion and bipolar disorder, which are not the focus of this current study [22–23].

Charlson Comorbidity Index

The Charlson Comorbidity Index is a validated measure of the number and severity of coexisting diagnoses. For each Veteran with FMS, we calculated the Charlson Comorbidity Index [12] using ICD-9-CM diagnostic codes related to inpatient and outpatient encounters during the 12 mo following the index FMS date [24].

Statistical Analysis

We examined frequency distributions of sociodemographic and military service characteristics among Veterans who met our FMS case definition and Veterans who had no FMS diagnoses from fiscal years 2002–2012, stratified by sex. We used the Pearson chi-square test to examine statistically significant differences in the distribution of these characteristics.

We examined associations between combined utilization of regular primary care with mental health and/or rheumatology care as a proxy for an interdisciplinary,

team-based approach (vs only primary care utilization) and the risk of ≥2 opioid or ≥2 nonopioid pain-related prescriptions in the 12 mo following the index FMS diagnosis. We restricted our analysis to Veterans with ≥1 primary care visit during the 12 mo of follow-up to avoid including Veterans who may have sought care only outside of the VHA. To examine these associations, we fit generalized linear models with a log-link, Poisson family (a log-Poisson regression model), and robust standard errors to estimate risk ratios (RRs) and 95 percent confidence intervals (CIs). The log-Poisson regression model with robust standard errors allows estimation of RRs for prospective studies with binary outcome data [25].

The following potential confounding variables were identified a priori and were included in all adjusted models, including Model 1: number of anxiety, PTSD, and depression diagnoses during the 12 mo after index FMS date and nonreferent indicator variables (i.e., dummy variables that excluded the reference category) for each mental health disorder (1, 2, and ≥3 diagnoses). We also adjusted for the Charlson Comorbidity Index (2 nonreferent indicator variables: 1 and ≥2). We used indicator variables to allow flexibility for fitting potential nonlinear associations. In Model 2, we additionally adjusted for sociodemographic and military characteristic variables: age at index FMS date (2 nonreferent indicator variables: >30–40 and >40); white, non-Hispanic race/ethnicity; married marital status; and greater than high school education as well as Active Duty status and branch of service (4 nonreferent indicator variables: Air Force, Navy, Marines Corps, and Coast Guard).

There have been temporal changes in the "VA/DOD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain" [26–27]. These may have resulted in changes to FMS management, including prescribing practices of opioid and nonopioid pain-related medications. We explored whether our results were sensitive to the adjustment for the year of index FMS diagnosis by including 10 nonreferent indicator variables for calendar years 2002–2011 [3,28]. We also explored whether adjustment for the index FMS setting (whether in a rheumatology setting) materially altered our results. Researchers have advised that for mental health diagnoses determined by ICD-9-CM codes, those who only have one diagnosis code may not truly have the mental health diagnosis [16]. To address this potential limitation, we also explored whether results for Model 1 were sensitive to recoding of individuals who had only one ICD-9-CM code corresponding to anxiety, PTSD, or depression as having no diagnosis.

All *p*-values were two-sided and defined to be significant at $p < 0.01$. All analyses were conducted using Stata software (version 12.1, StataCorp; College Station, Texas).

RESULTS

Prevalence and Characteristics of Veterans with FMS

The prevalence of FMS was higher among female than male Veterans. There were 5,963 (0.9%) male and 2,245 (2.5%) female Veterans, or 1 percent of male and female Veterans combined, with prevalent FMS according to our case definition among OIF/OEF/OND Veterans who had ≥1 VHA encounter from fiscal years 2002–2012. Compared with the 631,868 male and 86,640 female Veterans who did not have a FMS diagnosis during the 10 yr study period, Veterans with FMS were older, more likely to be Hispanic, and never or currently married, regardless of sex (**Table 1**). Females with FMS were more likely to have attained more than a high school education and to have served in the Air Force than females without FMS. Males with FMS were more likely to have served in the Army than males without FMS.

Outpatient Settings of Index FMS Diagnosis

Over a quarter of FMS diagnoses were documented in a primary care setting (24% for male and 29% for female Veterans) (**Table 2**). The other top five settings were similar for FMS diagnoses across male and female Veterans, including chiropractic care, physical medicine and rehabilitation, and rheumatology/arthritis specialty care settings. Eight percent of female Veterans with FMS received an index diagnosis in women's health-related specialty clinic settings. A higher proportion of male (11%) versus female (6%) Veterans received their index FMS diagnosis in a pain specialty clinic.

Utilization of Primary Care and Mental Health and Rheumatology Specialty Care

Among 4,855 male and 1,786 female Veterans with at least 12 mo of follow-up after their FMS index date, most male (n = 4,441 [91%]) and female (n = 1,526 [85%]) Veterans had ≥1 primary care encounter. Also, most male (n = 3,437 [71%]) and female (n = 1,299 [73%]) Veterans had ≥1 mental health encounter. Fewer

Table 1.
Sociodemographic and military service characteristics among Veterans, returned from Iraq and Afghanistan, who accessed Veterans Health Administration (VHA) care during fiscal years 2002–2012. Data presented as *n* (%).

Characteristic	Males With FMS (*n* = 5,963)	Males Without FMS (*n* = 631,868)	Females With FMS (*n* = 2,245)	Females Without FMS (*n* = 86,640)
Age Group at First VHA Encounter (yr)*				
18–30	2,734 (45.8)	343,440 (54.4)†	962 (42.9)	52,194 (60.2)†
>30–40	1,587 (26.6)	140,451 (22.2)	636 (28.3)	18,609 (21.5)
>40–50	1,295 (21.7)	115,101 (18.2)	519 (23.1)	12,677 (14.6)
>50–60	339 (5.7)	30,442 (4.8)	113 (5.0)	3,021 (3.5)
>60–75	7 (0.1)	2,262 (0.4)	6 (0.3)	136 (0.2)
Race*				
White	2,915 (48.9)	362,543 (57.4)†	776 (34.6)	38,790 (44.8)†
Black	555 (9.3)	70,817 (11.2)	449 (20.0)	18,963 (21.9)
Hispanic	767 (12.9)	583 (0.1)	235 (10.5)	55 (0.1)
Other	261 (4.4)	22,595 (3.6)	166 (7.4)	3,452 (4.0)
Marital Status*				
Never Married	2,427 (40.7)	199,276 (31.5)†	1,023 (45.6)	31,332 (36.2)†
Married	3,215 (53.9)	278,436 (44.1)	898 (40.0)	25,741 (29.7)
Divorced/Separated/Widowed	318 (5.3)	91,304 (14.4)	319 (14.2)	19,462 (22.5)
Education*				
≤High School	4,596 (77.1)	494,116 (78.2)	1,514 (67.4)	62,434 (72.1)†
>High School	1,285 (21.6)	129,833 (20.5)	700 (31.2)	22,983 (26.5)
Component				
Active Duty	3,003 (50.4)	349,351 (55.3)	1,232 (54.9)	48,615 (56.1)
National Guard/Reserve	2,960 (49.6)	282,517 (44.7)	1,013 (45.1)	38,025 (43.9)
Rank‡				
Enlisted	5,638 (94.6)	581,543 (92.0)†	2,055 (91.5)	78,397 (90.5)
Officer	254 (4.3)	43,720 (6.9)	169 (7.5)	7,726 (8.9)
Branch of Service‡				
Army	4,088 (68.6)	399,110 (63.2)†	1,443 (64.3)	55,392 (63.9)†
Air Force	585 (9.8)	63,726 (10.1)	452 (20.1)	14,325 (16.5)
Navy	552 (9.3)	74,282 (11.8)	301 (13.4)	13,408 (15.5)
Marine Corps	733 (12.3)	94,183 (14.9)	47 (2.1)	3,469 (4.0)

*Some values are "missing" or "unknown" for these characteristics.
†Some values for these characteristics are "other."
‡Chi-square test, comparison across FMS status ($p < 0.01$).
FMS = fibromyalgia syndrome.

male (*n* = 733 [15%]) and female (*n* = 516 [29%]) Veterans had ≥1 follow-up rheumatology specialty care visit.

For the 4,441 male and 1,526 female Veterans who had ≥1 primary care visit during the 12 mo following their index FMS diagnosis date, the median (range) of primary care encounters for male and female Veterans was 4 (1–54) and 4 (1–61) visits, respectively. The median (range) of mental health encounters for male and female Veterans was 5 (0–231) and 6 (0–183) visits, respectively. For rheumatology care encounters 12 mo following index FMS diagnosis date, the median (range) for male and female Veterans was 0 (0–13) and 0 (0–15) visits, respectively. Most Veterans (~80%) received a combination of primary care and mental health or a combination of primary care and rheumatology care (**Table 3**). A higher proportion of female (*n* = 357 [23%]) than male (*n* = 531 [12%]) Veterans received a combination of care from all three settings.

Associations of Combined Primary Care with Mental Health and/or Rheumatology Utilization and Pain-Related Medication Prescriptions

There were 1,830 (41%) males and 589 (39%) females who received ≥1 opioid prescription among Veterans with ≥1 primary care visit during the 12 mo following their index FMS diagnosis date. Most Veterans received

Table 2.
Top 10 fibromyalgia syndrome (FMS) outpatient care settings corresponding to index FMS diagnosis, restricted to Veterans who only had one unique stop code.*

Male Veterans (*n* = 5,692)		Female Veterans (*n* = 2,150)	
Top 10 Primary Stop Codes	***n* (%)**	**Top 10 Primary Stop Codes**	***n* (%)**
Primary Care: 342, 348, 350, or 323 (excluding secondary stop code 135)	1,367 (24.0)	Primary Care: 342, 348, 350, or 323 (excluding secondary stop code 135)	632 (29.4)
Chiropractic Care: 436	904 (15.9)	Rheumatology/Arthritis: 314	300 (14.0)
Physical Medicine & Rehabilitation: 201	829 (14.6)	Physical Medicine & Rehabilitation: 201	283 (13.2)
Pain Clinic: 420	595 (10.5)	Women's Health Clinic: 322, 339, 404, 426, 525, or 704	173 (8.0)
Rheumatology/Arthritis: 314	461 (8.1)	Chiropractic Care: 436	155 (7.2)
Polytrauma/Traumatic Brain Injury/Speech Pathology: 197 or 219	315 (5.5)	Pain Clinic: 420	131 (6.1)
Physical Therapy: 205	281 (4.9)	Polytrauma/Traumatic Brain Injury/Speech Pathology: 197 or 219	69 (3.2)
Complementary Alternative Medicine: 159	118 (2.1)	Physical Therapy: 205	63 (2.9)
Laboratory: 108	79 (1.4)	Mental Health: 502–524, 527–599, or 725–731	35 (1.6)
Neurology: 106, 126–128, 293, 315, 325, 335, 345, or 346	76 (1.3)	Neurology: 106, 126–128, 293, 315, 325, 335, 345, or 346	31 (1.4)
Other Outpatient Setting	462 (8.1)	Other Outpatient Setting	166 (7.7)

*13 males and 2 females were missing stop code associated with FMS index date/diagnosis; 258 males and 93 females had ≥2 unique stop code combinations associated with FMS index date/diagnosis.

Table 3.
Primary care, mental health, and rheumatology utilization 12 mo after index fibromyalgia syndrome date among Veterans who had at ≥1 primary care follow-up visit.*

Care Setting	Male Veterans (*n* = 4,441)	Female Veterans (*n* = 1,526)
Primary Care Only (*n*)	1,055 (23.8)	288 (18.9)
<4 Visits (%), reference category	695 (15.6)	173 (11.3)
≥4 Visits (%)	360 (8.1)	115 (7.5)
Primary Care & Mental Health, No Rheumatology (*n*)	2,706 (60.9)	787 (51.6)
<4 Primary Care Visits (%)	1,135 (25.6)	336 (22.0)
≥4 Primary Care Visits (%)	1,571 (35.4)	451 (30.0)
Primary Care & Rheumatology, No Mental Health (*n*)	149 (3.4)	94 (6.2)
<4 Primary Care Visits (%)	88 (2.0)	52 (3.4)
≥4 Primary Care Visits (%)	61 (1.4)	42 (2.8)
Combined Primary Care, Mental Health, & Rheumatology (*n*)	531 (12.0)	357 (23.4)
<4 Primary Care Visits (%)	186 (4.2)	124 (8.1)
≥4 Primary Care Visits (%)	345 (7.8)	233 (15.3)

*1,108 males and 459 females had <12 mo of follow-up, and 414 males and 260 females had no primary care visits; multiple visits can occur on same day only if visits are in different settings.

≥1 nonopioid pain-related prescription: 3,017 (68%) males and 1,124 (74%) females. The median (range) of opioid prescriptions for male and female Veterans was 3 (1–42) and 2 (1–26), respectively. The median (range) of nonopioid pain-related prescriptions for male and female Veterans was 2 (1–20) and 2 (1–21), respectively.

Contrary to our primary hypothesis, we found that compared with <4 primary care visits (i.e., less than regular primary care), combined regular primary care, mental health, and rheumatology utilization was associated with ≥2 opioid prescriptions: RRs and 95 percent CIs for male and female Veterans were 2.22 (1.13–4.39) and 2.79 (0.42–18.62), respectively, for the fully adjusted model (Model 2, **Tables 4**–**5**).

Supporting our secondary hypothesis, we did find evidence that compared with Veterans who received less

Table 4.
Associations of combined regular primary care and mental health and/or rheumatology utilization and pain-related medication prescriptions (opioid or nonopioid) 12 mo following index fibromyalgia syndrome (FMS) diagnosis date among **male** Veterans (n = 4,441).

Model Variable	<4 PC Visits Only	≥4 PC Visits Only	≥4 PC Visits & MH	≥4 PC Visits & RH	≥4 PC Visits, MH & RH
No. at Risk	695	360	1,571	61	345
No. with ≥2 Opioid Rx	75	78	662	9	151
RR (95% CI)					
Unadjusted	1.0 (reference)	2.01 (1.50–2.68)	3.90 (3.13–4.87)	1.37 (0.72–2.59)	4.06 (3.17–5.18)
Model 1*	1.0 (reference)	1.40 (0.71–2.75)	1.77 (1.06–2.98)	0.97 (0.26–3.58)	1.82 (1.07–3.09)
Model 2†	1.0 (reference)	2.02 (0.89–4.57)	2.20 (1.13–4.29)	1.04 (0.17–6.45)	2.22 (1.13–4.39)
No. with ≥2 Nonopioid Rx	59	67	1,001	20	245
RR (95% CI)					
Unadjusted	1.0 (reference)	2.19 (1.58–3.04)	7.51 (5.86–9.61)	3.86 (2.50–5.96)	8.37 (6.49–10.78)
Model 1*	1.0 (reference)	2.60 (1.14–5.91)	4.50 (2.21–9.15)	2.37 (0.71–7.89)	4.92 (2.41–10.05)
Model 2†	1.0 (reference)	3.42 (0.98–11.88)	6.99 (2.32–21.09)	2.02 (0.27–15.11)	7.79 (2.57–23.57)

*Model 1 is adjusted for no. anxiety diagnoses (1, 2, ≥3), no. posttraumatic stress disorder diagnoses (1, 2, ≥3), no. depression diagnoses (1, 2, ≥3), and Charlson Comorbidity Index (1, ≥2); each value is included as an indicator variable.
†Model 2 adjusts for same variables in Model 1 in addition to sociodemographic variables: age at FMS index date (2 indicator variables: >30–40, >40), white non-Hispanic race/ethnicity, married marital status, greater than high school education, and military characteristics: Active Duty, branch of service (4 indicator variables: Air Force, Navy, Marine Corps, Coast Guard).
CI = confidence interval, MH = mental health, No. = number, PC = primary care, RH = rheumatology, RR = risk ratio, Rx = prescription.

Table 5.
Associations of combined primary care and mental health and/or rheumatology utilization and pain-related medication prescriptions (opioid or nonopioid) 12 mo following index fibromyalgia syndrome (FMS) diagnosis date among **female** Veterans (n = 1,526).

Model Variable	<4 PC Visits Only	≥4 PC Visits Only	≥4 PC Visits & MH	≥4 PC Visits & RH	≥4 PC Visits, MH & RH
No. at Risk	173	115	451	42	233
No. with ≥2 Opioid Rx	14	21	155	10	78
RR (95% CI)					
Unadjusted	1.0 (reference)	2.26 (1.20–4.25)	4.25 (2.53–7.13)	2.94 (1.41–6.16)	4.14 (2.43–7.06)
Model 1*	1.0 (reference)	2.59 (0.28–23.57)	3.95 (0.61–25.67)	—‡	3.89 (0.60–25.50)
Model 2†	1.0 (reference)	2.12 (0.24–18.55)	2.95 (0.45–19.30)	—‡	2.79 (0.42–18.62)
No. with ≥2 Nonopioid Rx	24	27	300	16	169
RR (95% CI)					
Unadjusted	1.0 (reference)	1.69 (1.03–2.78)	4.79 (3.29–6.99)	2.75 (1.61–4.69)	5.23 (3.58–7.64)
Model 1*	1.0 (reference)	1.65 (0.44–6.14)	3.15 (1.14–8.77)	1.91 (0.50–7.36)	3.38 (1.22–9.41)
Model 2†	1.0 (reference)	1.03 (0.26–4.12)	2.19 (0.82–5.87)	0.85 (0.21–3.45)	2.32 (0.87–6.21)

*Model 1 is adjusted for no. anxiety diagnoses (1, 2, ≥3), no. posttraumatic stress disorder diagnoses (1, 2, ≥3), no. depression diagnoses (1, 2, ≥3), and Charlson Comorbidity Index (1, ≥2); each value is included as an indicator variable.
†Model 2 adjusts for same variables in Model 1 in addition to sociodemographic variables: age at FMS index date (2 indicator variables: >30–40, >40), white non-Hispanic race/ethnicity, married marital status, greater than high school education, and military characteristics: Active Duty, branch of service (4 indicator variables: Air Force, Navy, Marine Corps, Coast Guard).
‡Too few events limited risk estimation.
CI = confidence interval, MH = mental health, No. = number, PC = primary care, RH = rheumatology, RR = risk ratio, Rx = prescription.

than regular primary care (<4 primary care visits in the 12 mo after index FMS date), combined regular primary care, mental health, and rheumatology utilization was associated with ≥2 nonopioid pain-related prescriptions: RRs and 95 percent CIs for male and female Veterans were 7.79 (2.57–23.57) and 2.32 (0.87–6.21), respectively, for the fully adjusted model (Model 2, **Tables 4–5**).

These results were not materially altered when we further adjusted for the year of index FMS diagnosis and whether the index diagnosis was in a rheumatology setting (**Appendix 2**, available online only). Also, our results were robust to recoding of individuals with one diagnosis of anxiety, PTSD, or depression to having no diagnosis for these conditions.

DISCUSSION

To the best of our knowledge, this is the first study to report the prevalence and related sociodemographic and military characteristics of FMS among national OIF/OEF/OND Veterans. We report a 10 yr FMS prevalence of 0.9 percent among males and 2.4 percent among females who accessed the VHA. Over a quarter of FMS diagnoses were documented in a primary care setting. Compared with Veterans without FMS, Veterans with FMS were more likely to be female, older, never/currently married, and to have served in the Army (males) or Air Force (females). One year following index FMS diagnosis, most Veterans sought a combination of primary care and mental health and/or rheumatology. Contrary to our primary hypothesis, Veterans with FMS with regular primary care visits combined with mental health and rheumatology visits were more likely to be prescribed ≥2 opioids during the 12 mo following index FMS diagnosis. Combined care was also associated with ≥2 nonopioid pain-related prescriptions.

The prevalence of FMS in our study of OIF/OEF/OND Veterans was within the range reported in studies of civilian [1] and military populations [3]. Researchers have reported that among Gulf war Veterans, deployment (versus nondeployment) may be associated with a doubling of the risk of FMS (odds ratio 2.32 [95% CI: 1.02–5.27]) [29]. The present study did not examine the association between deployment and FMS diagnosis. Other characteristics that we found to be related to FMS diagnoses were consistent with prior studies, including older age and female sex [1,3,5,14]. The FMS-female sex association is worth noting because women continue to be one of the fastest growing subsets of VHA users [30]. We are unaware of prior studies that report a higher prevalence of FMS among those of Hispanic ethnicity, though there are limited investigations of race/ethnicity and FMS. Studies of chronic pain in general support that Hispanic and African American race/ethnicities are at greater risk of experiencing pain, but it is unclear that these differences remain after controlling for other confounding variables [31]. If our findings are replicated, they may provide evidence for potential disparities in the experience of FMS and FMS management among ethnic minorities. Identification of disparities in pain and pain management has been highlighted as an area of needed future research in the Institute of Medicine's "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research" [32].

Consistent with a prior non-VHA study of FMS, FMS diagnoses were most common in primary care [15]. In our study of the VHA, other predominant nonrheumatology clinical settings of FMS diagnoses included chiropractic care, physical medicine and rehabilitation, and pain clinics. Also, among females, women's health-related clinics were one of the top five settings of FMS diagnoses. Since most diagnoses of FMS occur outside the rheumatology setting, it may be important to ensure that clinicians in these settings are made aware of and trained in the latest evidence-based practice guidelines for diagnosing and managing FMS and that procedures are in place for timely referrals to rheumatology, especially if a diagnosis is elusive [10]. Some experts recommend that rheumatologists train primary care colleagues on the recognition of FMS [33].

Investigators have demonstrated that patients with FMS in both civilian and military populations have higher utilization of healthcare. Berger et al. reported that compared with civilians without FMS, those with FMS had twice as many outpatient and four times as many emergency room visits over 12 mo [14]. Other investigators have reported that utilization of healthcare is higher for FMS than other chronic medically unexplained symptoms among military personnel, including irritable bowel syndrome and chronic fatigue syndrome [3]. Therefore, it may not be surprising that in the present study most Veterans sought a combination of primary care and mental health and/or rheumatology specialty care 12 mo following their index FMS diagnosis; this was especially evident for combined primary care with mental health.

Whether utilization of combined care in our study is a reflection of a guideline-recommended, interdisciplinary, team-based approach; comorbid diagnoses; and/or challenges related to identifying and managing FMS is uncertain. On the one hand, FMS is known to be associated with a number of comorbid conditions; seven conditions were reported by investigators of a civilian population-based study, including depression, anxiety, headache, irritable bowel syndrome, chronic fatigue syndrome, systemic lupus erythematous, and rheumatoid arthritis [5]. Each of these conditions was 2 to 7 times more likely to be present in patients with FMS than patients without FMS. PTSD is another condition that is often comorbid with FMS and highly prevalent in the OIF/OEF/OND Veteran population [11,34–37]. While we

did not examine all reported comorbid conditions of FMS, we did examine mental health-related conditions. The prevalence of ≥1 diagnosis for anxiety, PTSD, and depression 12 mo following index FMS date was 21.5, 51.0, and 21.0 percent, respectively. Restricting to individuals with ≥2 diagnoses reduced these prevalence estimates by 5 percent. The combined utilization of primary care with mental health among Veterans in our study may be expected given the high prevalence of mental health conditions. On the other hand, combined care may be a reflection of high healthcare utilization overall, which may indicate complexity of the patients, poor coordination of care, and challenges related to diagnosing FMS [7,10,38]. We did not examine overall healthcare utilization of Veterans seeking combined care (vs those with primary care visits only), nor could we examine the reasons for follow-up utilization. As a result, it is unclear whether combined utilization represents recommended interdisciplinary, team-based approaches for managing FMS; higher utilization of services to independently address the multiple comorbid conditions [11]; or perhaps overutilization of VHA care. Lastly we note that stop codes, for mental health services in particular, likely reflect various levels of interdisciplinary and integrative treatment, which the current study could not examine.

We sought empiric evidence to support the clinical practice guideline recommendations that combined care is associated with best practices, i.e., less opioid use and more use of nonopioid pain-related medication. Contrary to our first hypothesis, results support associations of combined care with a higher risk of receiving ≥2 opioid prescriptions. We note that this finding is correlational, and we are unable to infer a direction of causality. Bearing this in mind, there are several potential explanations for our findings. The association between indicators of combined care and opioid therapy is consistent with clinical practice guidelines for opioid therapy [28]. Also, it may be that patients who receive opioid therapy are those with more complex, severe, and treatment-refractory conditions. Thus, the evidence for an association between combined care and opioid therapy may be consistent with a prior escalation of care in the service of attempting to better manage pain.

Our study robustly supports the hypothesis that Veterans with utilization of mental health and rheumatology in addition to regular primary care are more likely to be prescribed ≥2 nonopioid pain-related medications (guideline-adherent practice). For instance, when we explored a change in our reference category to "only regular primary care" users (rather than *less* than "only regular primary care" users), associations between combined regular primary care, mental health, and rheumatology utilization and ≥2 nonopioid pain-related medications remained statistically significant (**Appendix 2**, Model 2). In contrast, there is less evidence supporting that Veterans with combined care are more likely to be prescribed opioids (not consistent with guideline recommendations). When we explored a change in our reference category to "only regular primary care" users, the association of combined care and opioid use was no longer statistically significant. Thus, it may be that regular or greater primary care utilization (compared with *less* than regular primary care utilization) and not combined care per se is associated with higher likelihood of being prescribed opioids, perhaps due to other indications for opioid prescription and the necessary, regular encounters to responsibly manage the opioid use.

LIMITATIONS

As with all studies that rely on administrative data, there is the potential for misclassification of FMS. Since we were interested in focusing our analyses on Veterans with true diagnoses of FMS, we required that Veterans have ≥2 ICD-9-CM diagnoses of FMS in a 12 mo period or ≥1 diagnosis in a rheumatology specialty care setting. Although this definition has not been examined for validity in the OIF/OEF/OND Veteran population, similar definitions have been used in studies of military personnel and our prevalence estimates in male and female Veterans are similar to those reported previously [3]. Another weakness was that we were unable to determine the incident date of FMS diagnosis, which precluded analyses of causal relationships and limited our interpretation of temporal relationships. We relied on an index FMS diagnosis date, the first documentation of FMS in VHA diagnosis codes over the study period.

Interpretation of the results related to the examination of healthcare utilization and treatment during the 12 mo following the index FMS date should be made in the context of several potential limitations. These include use of combined utilization of regular primary care with mental health and/or rheumatology care as a proxy for an interdisciplinary, team-based approach to FMS care. We are uncertain whether this proxy is appropriate or

whether it is a reflection of escalated care utilization driven by patient need that is not interdisciplinary or integrative in nature. Since we did not examine reasons (including diagnoses) related to follow-up primary care, mental health, and rheumatology visits, we cannot make strong assertions regarding the potential benefit or harm of combined care for FMS. Second, we did not account for the potential variability in the specific knowledge or clinical expertise of the providers, which may be a valuable area for future research. Third, since we were unable to identify an explicit definition of regular primary care for FMS in the current "VA/DOD Clinical Practice Guideline for the Management of Chronic Multisymptom Illness" [17], we used the median number of visits in 12 mo, ≥4 primary care visits, to define "regular primary care," which may not be clinically relevant or may have limited generalizability. We note that our definition of "regular primary care" as ≥4 primary care visits/yr is consistent with some previous studies of management of somatoform disorders [39]. Fourth, although we attempted to control for potential confounding variables, there may be residual confounding, which if present would bias our estimates of risk. To ensure that we had adequate power to estimate RRs, we used the medians (among Veterans with medication use) for analyses of pain-related medication associations. However, especially for the analyses of opioids, a more clinically relevant outcome may be chronic use. Because we did not have details on dose or longitudinal duration of continued or intermittent treatment, we were unable to examine chronic use. Also, we used prescription history as noted in the electronic medical record as an indicator for medication use; we did not determine whether patients actually consumed their medications or how adherent they were to prescription instructions. We were unable to examine the clinical indication for the medication prescriptions. For example, some of the nonopioid pain-related medications, antidepressants and gabapentinoids, in particular, may have been prescribed for the management of nonpain medical and mental health comorbidities that are common among patients with FMS. There may have been losses to follow-up, which could introduce selection bias, although we attempted to address this by including only Veterans with ≥1 primary care visit through the VHA during the 12 mo following FMS index date. Future investigations are needed to examine other guideline-recommended treatments for FMS, including patient education, graded exercise, cognitive behavioral therapy, and complementary and alternative medicine therapies.

CONCLUSIONS

Our present study extends the current scope of research on FMS to include OIF/OEF/OND Veterans who access VHA. Our study confirmed several previously identified risk factors for FMS and identified potential new risk factors (e.g., Hispanic ethnicity) that warrant further investigation. Contrary to our hypothesis, Veterans with FMS who utilized regular primary care, mental health, and rheumatology (combined care) were more likely to be prescribed opioids. However, closer examination suggests that regular primary care (relative to less than regular primary care) is driving the association. Combined care was also associated with ≥2 nonopioid pain-related prescriptions; unlike the findings for opioid medications, results were not materially altered in our sensitivity and exploratory analyses. Future studies are needed to more closely examine associations of interdisciplinary, team-based approaches to FMS care, overall VHA utilization, and recommendations for FMS treatment. Such studies can support the implementation of evidence-based management of FMS in VHA.

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Iraq and Afghanistan Veterans report symptoms consistent with chronic multisymptom illness one year after deployment

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Abstract—Many Veterans returning from service in Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) experience chronic pain. What is not known is whether for some OIF/OEF Veterans this pain is part of a larger condition of diffuse multisystem symptoms consistent with chronic multisymptom illness (CMI). We use data from a prospective longitudinal study of OIF/OEF Veterans to determine the frequency of CMI. We found that 1 yr after deployment, 49.5% of OIF/OEF Veterans met criteria for mild to moderate CMI and 10.8% met criteria for severe CMI. Over 90% of Veterans with chronic pain met criteria for CMI. CMI was not completely accounted for either by posttraumatic stress disorder or by predeployment levels of physical symptoms. Veterans with symptoms consistent with CMI reported significantly worse physical health function than Veterans who did not report symptoms consistent with CMI. This study suggests that the presence of CMI should be considered in the evaluation of OIF/OEF Veterans. Further, it suggests that the pain management for these Veterans may need to be tailored to take CMI into consideration.

Key words: chronic multisymptom illness, chronic pain, combat deployment, mental health function, Operation Iraqi Freedom/Operation Enduring Freedom, pain management, Persian Gulf war, physical health function, PTSD, Veterans.

INTRODUCTION

Chronic pain is a significant and complex problem for Veterans who deployed to Iraq (Operation Iraqi Freedom [OIF]) and Afghanistan (Operation Enduring Freedom [OEF]). Forty-three percent of OIF/OEF Veterans seeking treatment at a Department of Veterans Affairs (VA) hospital reported pain, with 63 percent of those Veterans reporting clinically significant pain [1]. Further,

Abbreviations: ANCOVA = analysis of covariance, CDC = Centers for Disease Control and Prevention, CMI = chronic multisymptom illness, HEROES = Healthy Resilience after Operational and Environmental Stressors, MCS = mental health composite score, mTBI = mild traumatic brain injury, OEF = Operation Enduring Freedom, OIF = Operation Iraqi Freedom, PCS = physical health composite score, PHQ-15 = Patient Health Questionnaire-15, PTSD = posttraumatic stress disorder, VA = Department of Veterans Affairs, VR-36 = Veterans RAND 36-Item Health Survey.

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OIF/OEF Veterans with chronic pain have worse physical health function than OIF/OEF Veterans without chronic pain [2]. Finally, OIF/OEF Veterans with chronic pain are more likely to present with another postdeployment health condition (i.e., posttraumatic stress disorder [PTSD], mild traumatic brain injury [mTBI], and/or polysubstance abuse) [3] than to present with only chronic pain. What is not known is how often chronic musculoskeletal pain presents with other chronic and comorbid symptoms, such as chronic fatigue, gastrointestinal distress, or cognitive problems such as difficulty finding words. It is possible that for some OIF/OEF Veterans, chronic pain may be only one symptom of a larger multisymptom syndrome. Walker et al. suggested that the most common health concern of OIF/OEF Veterans are diffuse, widespread, and overlapping physical, cognitive, and emotional symptoms [4].

There is good reason to suspect that some OIF/OEF Veterans with chronic pain are also experiencing other chronic symptoms. Multisystem diffuse symptoms have been common in Veterans after every modern war [5–6]. This was particularly clear after the Persian Gulf war (Operation Desert Shield/Operation Desert Storm), when an estimated 30 percent of Veterans experienced multiple chronic symptoms [7–10]. Termed chronic multisymptom illness (CMI) (or Gulf War Illness), the Centers for Disease Control and Prevention (CDC) defines CMI as having one or more chronic symptoms (≥6 mo duration) from two or more symptom categories: (1) fatigue, (2) mood and cognition (e.g., concentration problems, depression), or (3) musculoskeletal (e.g., joint pain) [11]. Evidence has found that CMI is distinct from PTSD or depression [12]. CMI causes disability that is as severe as found in other chronic illnesses and continues to affect Persian Gulf war Veterans many years after their deployment [7,13].

There is preliminary evidence to suggest that OIF/OEF Veterans may also be experiencing increases in widespread symptoms. Three cross-sectional studies found heightened physical symptom severity as measured with the Patient Health Questionnaire-15 (PHQ-15). Iverson et al. reported that 41 percent of women and 31 percent of men deployed to OIF/OEF reported medium or higher levels of physical symptom severity [14]. McAndrew et al. reported on the relationship between physical symptoms and environmental exposure concerns among OIF/OEF Veterans seeking care at a VA tertiary clinic [15]. They found, on average, medium levels of physical symptom severity, and symptom severity was positively associated with environmental exposure concerns [15]. Similarly, Hoge et al. found, on average, medium levels of physical symptom severity among OIF/OEF Veterans and higher symptom severity among OIF/OEF Veterans with PTSD [16]. Medium levels of symptoms are associated with a greater number of physician visits and more disability days [17].

Especially compelling evidence comes from the Millennium Cohort Study. The Millennium Cohort Study is a prospective longitudinal study of 73,078 OIF/OEF military personnel [18], which used a close approximation of the CDC definition of CMI with some modifications (e.g., two instead of three pain symptoms, "unusual fatigue" instead of general fatigue). Comparing military personnel who deployed with those who did not deploy, this study found that combat deployment resulted in a 1.7 times increase in odds of meeting CMI criteria. Further, an estimated 26.5 percent of OIF/OEF Veterans who deployed met criteria for CMI after deployment. These data suggest that CMI is a problem among OIF/OEF Veterans, a view also suggested by the Institute of Medicine [19]. These existing studies are limited by not having used the specific CDC definition; thus, we do not yet know whether OIF/OEF Veterans meet that definition of CMI. Further, no existing study has used a pre-post deployment longitudinal design that provides the ability to assess whether symptoms increase after combat deployment or whether OIF/OEF soldiers could have been experiencing heightened symptoms prior to combat deployment.

To optimally address pain among OIF/OEF Veterans, it is critical that we understand whether CMI is a problem among these Veterans, and if so, its relationship to chronic pain. The presence of chronic pain in the context of CMI likely necessitates modification of pain management treatments. Focusing exclusively on chronic pain without taking into account the patients' other symptoms may lead to poor adherence to treatment recommendations and low satisfaction with care. Similarly, treatments for CMI need to be tailored when the predominant symptom is pain as compared with when the predominant symptoms are fatigue or gastrointestinal distress.

The goal of the current study was to report the frequency of CMI in soldiers returning from war using data from a longitudinal, prospective study, the Healthy Resilience after Operational and Environmental Stressors (HEROES) Project. The HEROES Project improves upon

limitations of past studies by using the CDC definition of CMI and using a pre-post deployment longitudinal design. The aims of the current study were to—

1. Estimate the frequency of OIF/OEF Veterans who report symptoms consistent with CMI at 1 yr postdeployment.
2. Examine the relationship between CMI at 1 yr postdeployment and chronic pain symptoms at 1 yr postdeployment, PTSD symptoms at 1 yr postdeployment, and physical symptom severity at predeployment.
3. Determine the relationship of CMI assessed at 1 yr postdeployment to physical and mental health function at 1 yr postdeployment, controlling for physical symptom severity and health function at predeployment and PTSD symptoms at 1 yr postdeployment.

METHODS

The HEROES Project is a prospective longitudinal observational cohort design with measures collected at four time points: predeployment, immediately postdeployment, 3 mo postdeployment, and 1 yr postdeployment (for description see McAndrew et al., Yan et al., and Quigley et al. [20–22]).

Participants

Participants were Army National Guard and Army Reserve enlisted soldiers (including noncommissioned officers) deploying to either OIF or OEF who participated in the HEROES Project [20–22]. Exclusion criteria were current self-reported depression, medications with cardiovascular and/or autonomic effects (e.g., beta blockers or other antihypertensive medication), history of schizophrenia or bipolar disorder or current cancer, high blood pressure, or pregnancy. The larger study included a physiological assessment (not reported here) that necessitated excluding patients on medications with cardiovascular and/or autonomic effects and those with high blood pressure.

At the 1 yr postdeployment assessment, 319 soldiers completed the questionnaire on CMI. This was from an initial study sample of 795 soldiers (at predeployment). Out of the initial sample, 32 did not mobilize, were officers, or were severely injured or killed in action. At 1 yr postdeployment, 118 participants declined to participate (14.8%). The remainder of the participants whose data were missing at 1 yr postdeployment were lost to follow-up. Most of these were lost to follow-up because we did not receive information on when they returned from deployment (n = 289); for the others we do not have information on the reasons they were lost to follow-up (n = 37). Physical symptom severity at baseline was not related to the likelihood of being lost to follow-up at 1 yr postdeployment ($X^2 = 0.80$, $p = 0.85$).

Procedure

Study personnel approached soldiers who had just finished their medical processing or were waiting to complete their medical processing. We emphasized the voluntary nature of their participation and that research staff were civilian VA personnel. We examined differences between those who volunteered and those who declined to participate. There was no significant difference in the proportion of males and females in the participant and nonparticipant groups ($X^2 = 2.30$, $p = 0.13$). However, using a dichotomized variable for general health (excellent/very good vs good/fair/poor), there was a small but statistically significant difference between the participant sample and the nonparticipant sample. There were fewer individuals reporting excellent/very good health in the participant sample (72.1% of participant sample vs 78.8% of nonresponse sample; $X^2 = 8.25$, $p < 0.01$). We choose to ask about general health because it was only one item and has previously been shown to prospectively predict health.

Following recruitment, soldiers were given information about the study and screened for eligibility, and those who were eligible and interested gave informed consent. Soldiers completed predeployment self-report questionnaires and physiological measures (not included here) while at the Army installation. Immediately postdeployment, soldiers again completed self-report questionnaires at the Army installation. Soldiers who did not return to their installation were sent the immediate postdeployment questionnaires via mail. Data at 3 mo and 1 yr postdeployment were collected through mailed questionnaires. This report focuses on self-report of CMI measured at 1 yr postdeployment controlling for predeployment factors. The protocol was approved by Institutional Review Boards of the VA (VA New Jersey Healthcare System and the G.V. [Sonny] Montgomery VA Medical Center) and by the Walter Reed Department of Clinical Investigation.

Measures

Chronic Multisymptom Illness

CMI was assessed at 1 yr after deployment using the CDC definition. The Institute of Medicine recently released a report that reviewed the evidence for a case definition of CMI. They recommended using either the CDC definition or the Kansas definition [23–24] because both encompassed most of the symptoms of CMI. We chose to use the CDC definition because it provided a broader definition of CMI and can more easily be assessed through self-report because the Kansas definition requires assessment of possible medical exclusions. To meet the CDC criteria for CMI, participants are asked about the severity (mild, moderate, or severe) and duration (≥6 mo duration) of 10 common symptoms. CMI is defined as having one or more chronic symptoms (≥6 mo duration) from two or more symptom categories. The three symptom categories are (1) fatigue, (2) mood and cognition (symptoms of feeling depressed, difficulty remembering or concentration, feeling moody, feeling anxious, trouble finding words, or difficulty sleeping), and (3) musculoskeletal (symptoms of joint pain, joint stiffness, or muscle pain). We classified participants as having severe CMI if at least one symptom in two or more categories was rated as severe. We also asked about 25 additional symptoms that do not contribute to the definition of CMI. The prevalence of both CMI and these other symptoms is presented in **Table 1**.

Patient Health Questionnaire-15

Physical symptom severity was assessed at predeployment with the PHQ-15 [17]. Participants were asked to indicate, "During the past 7 days, how much have you been bothered by any of the following problems." Each item is scored as 0 (not bothered at all), 1 (bothered a little), or 2 (bothered a lot). Generally, cut offs of 0–4 (minimal), 5 (low), 10 (medium), and 15 (high) are used to create physical symptoms severity categories [17]. Items include stomach pain; back pain; pain in arms, legs, or joints; menstrual cramps or other problems with periods; headaches; chest pain; dizziness; fainting spells; feeling the heart pound or race; shortness of breath; pain or problems during sexual intercourse; constipation; loose bowels or diarrhea; nausea; gas or indigestion; feeling tired or having low energy; and trouble sleeping.

Health Function—Veterans RAND 36-Item Health Survey

The Veterans RAND 36-Item Health Survey (VR-36) is a measure of mental and physical health function [25–27] and was assessed at predeployment and 1 yr postdeployment. The VR-36 was developed from the 36-Item Short Form Health Survey. The VR-36 provides two composite scores, physical function (physical health composite score [PCS]) and mental function (mental health composite score [MCS]). These composite scores are composed of eight subscale scores: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. Composite and subscale scores are normed to a mean of 50 and a standard deviation of 10.

Posttraumatic Stress Disorder Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition

PTSD symptoms were assessed at 1 yr postdeployment with the Posttraumatic Stress Disorder Checklist-Civilian, which assesses for 17 symptoms of PTSD [28–29]. Participants were asked to indicate "in the past month, how much were you bothered by" each of 17 symptoms. Items are scored on a scale of 1 to 5. A score of 50 or greater is commonly used to denote significant PTSD symptoms [30].

Analysis

We first provide the frequency of CMI and specific physical symptoms at 1 yr postdeployment. A Pearson correlation was used to examine the relationship between CMI and age. Chi-square analyses were used to examine the relationship of CMI to sex and whether or not a participant had previously deployed, which prior research found to be related to increases in physical symptoms [31].

We next report the percentage of Veterans with musculoskeletal chronic pain who met criteria for CMI. To measure chronic pain, we used the musculoskeletal category of the CMI measure (≥1 symptoms of joint pain, joint stiffness, and muscle pain). We considered not including joint stiffness, but only eight Veterans reported joint stiffness without joint or muscle pain. Chi-square analyses were conducted to understand the relationship of chronic pain to CMI. Chi-square analyses were also used to examine the relationship of CMI to PTSD symptoms at 1 yr postdeployment and CMI to predeployment physical symptoms.

Table 1.
Operation Iraqi Freedom/Operation Enduring Freedom soldiers reporting symptoms with duration of greater than 6 mo at 1 yr after return from deployment, *n* (%). Bolded items are symptoms of chronic multisymptom illness from Centers for Disease Control and Prevention definition.

Symptom	Mild	Moderate	Severe	Total
Sinus Congestion	43 (13.5)	38 (12.0)	15 (4.7)	96 (30.0)
Headache	46 (14.4)	35 (11.0)	34 (10.7)	115 (36.1)
Fatigue	**55 (17.2)**	**50 (15.7)**	**21 (6.6)**	**126 (39.5)**
Joint Pain	**51 (16.0)**	**69 (22)**	**28 (8.8)**	**148 (46.0)**
Difficulty Remembering or Concentrating	**60 (18.8)**	**42 (13.2)**	**25 (7.8)**	**127 (39.8)**
Joint Stiffness	**40 (12.5)**	**50 (15.7)**	**18 (5.6)**	**108 (33.9)**
Difficulty Sleeping	**44 (13.8)**	**68 (21.3)**	**52 (16.3)**	**164 (51.4)**
Gas, Bloating, Cramps, or Abdominal Pain	20 (6.3)	25 (7.8)	10 (3.1)	55 (17.2)
Trouble Finding Words	**34 (10.7)**	**24 (7.5)**	**15 (4.7)**	**73 (22.9)**
Moody or Irritable	**65 (20.4)**	**61 (19.1)**	**36 (11.3)**	**162 (50.8)**
Rash or Sores	11 (3.4)	11 (3.4)	5 (1.6)	27 (8.5)
Numbness or Tingling	31 (9.7)	24 (7.5)	6 (1.9)	61 (19.1)
Muscle Pain	**31 (9.7)**	**33 (10.3)**	**7 (2.2)**	**71 (22.2)**
Hay Fever or Allergies	27 (8.5)	21 (6.6)	15 (4.7)	63 (19.7)
Feeling Depressed	**48 (15.0)**	**27 (8.5)**	**16 (5.0)**	**91 (28.5)**
Diarrhea (>3 loose stool samples per 24 h)	15 (4.7)	14 (4.4)	6 (1.9)	35 (11.0)
Sore Throat	9 (2.8)	3 (0.9)	0 (0)	12 (3.8)
Cough	25 (7.8)	8 (2.5)	4 (1.3)	37 (11.6)
Feeling Anxious	**44 (13.8)**	**43 (13.5)**	**19 (6.0)**	**106 (33.2)**
Unintentional Weight Gain ≥10 lb	24 (7.5)	36 (11.3)	15 (4.7)	75 (23.5)
Shortness of Breath	22 (6.9)	17 (5.3)	6 (1.9)	45 (14.1)
Chest Pain	15 (4.7)	9 (2.8)	3 (0.9)	27 (8.5)
Decreased Interest in Sex	21 (6.6)	15 (4.7)	14 (4.3)	50 (15.7)
Dizziness or Trouble Maintaining Balance	21 (6.6)	9 (2.8)	4 (1.3)	34 (10.7)
Night Sweats that Soak Bed Sheets	13 (4.1)	14 (4.4)	10 (3.1)	37 (11.6)
Fatigue Lasting 24 h After Exertion	18 (5.6)	11 (3.4)	9 (2.8)	38 (11.9)
Nasal Sores	4 (1.3)	5 (1.6)	0 (0)	9 (2.8)
Swollen Lymph Nodes	4 (1.3)	2 (0.6)	3 (0.9)	9 (2.8)
Milk Intolerance	7 (2.2)	8 (2.5)	7 (2.2)	22 (6.9)
Episodes of Disorientation	14 (4.4)	5 (1.6)	2 (0.6)	21 (6.6)
Nausea and Vomiting	8 (2.5)	5 (1.6)	3 (0.9)	16 (5.0)
Wheezing	6 (1.9)	9 (2.8)	1 (0.3)	16 (5.0)
Chemical Sensitivity	5 (1.6)	6 (1.9)	3 (0.9)	14 (4.4)
Fever	5 (1.6)	3 (0.9)	1 (0.3)	9 (2.8)
Unintentional Weight Loss >10 lb	5 (1.6)	1 (0.3)	3 (0.9)	9 (2.8)

Finally, we were interested in the relationship of CMI to health function. We first graphically depicted health function scores for each subscale of the VR-36 at three levels of CMI (no CMI, mild to moderate CMI, and severe CMI). We then used two analyses of covariance (ANCOVAs) to examine the relationship of CMI (no CMI, mild to moderate CMI, and severe CMI) to a composite score of mental health function (MCS) and a composite score of physical health function (PCS). Generally, a 2 to 3 point difference on these scores is considered clinically significant. In both models, we respectively controlled for the MCS or PCS at predeployment and the physical symptom severity from the PHQ-15 at predeployment. Examining postdeployment health function while controlling for predeployment levels of health function allows us to understand the relationship of CMI to postdeployment health function independent of predeployment levels. Similarly, controlling for predeployment physical symptoms allows us to understand the effect of symptoms that emerge after deployment (controlling for pre-existing symptom severity) on health function. We also controlled for PTSD symptoms at 1 yr

postdeployment, age, and sex because these also are related to health function.

RESULTS

Prevalence of Chronic Multisymptom Illness

At 1 yr after return from deployment, physical symptoms were assessed using the CDC measure of CMI; 46.7 percent reported physical symptoms consistent with CMI, and 10.8 percent reported symptoms consistent with severe CMI. Reporting physical symptoms consistent with CMI at 1 yr after return from deployment was not related to sex (X^2 = 1.49, p = 0.47) or to having deployed previously (X^2 = 2.89, p = 0.24). Meeting CMI criteria was related to greater age (r = 0.19, p < 0.01).

Physical Symptoms in Those with Chronic Multisymptom Illness

The prevalence of the 10 chronic (duration ≥6 mo) physical symptoms that define CMI at 1 yr postdeployment are listed in **Table 1** (in bold). The severity and duration of an additional 25 physical symptoms are listed in **Table 1**. The most common symptoms were difficulty sleeping (51.4%), being moody or irritable (50.8%), joint pain (46.0%), fatigue (39.5%), difficulty remembering or concentrating (39.8%), headaches (36.1%), and sinus congestion (30.0%).

Relationship of Chronic Multisymptom Illness to Pain Symptoms

We compared the number of Veterans who reported chronic musculoskeletal pain symptoms (defined as reporting either joint pain, joint stiffness, or muscle pain lasting 6 mo or longer) with the number of Veterans who reported symptoms consistent with CMI. We found a total of 166 (52%) Veterans reported chronic musculoskeletal pain, and 150 of these Veterans or 90 percent of those with musculoskeletal pain also met criteria for CMI. Thus, the vast majority of those reporting chronic musculoskeletal pain met criteria for CMI. Further, 82 percent of those who met criteria for CMI reported chronic pain (X^2 = 291.83, p < 0.01).

Relationship of Chronic Multisymptom Illness to Posttraumatic Stress Disorder

At 1 yr postdeployment, almost all Veterans who reported symptoms consistent with PTSD also reported symptoms consistent with CMI or severe CMI (X^2 = 47.27, p < 0.01). Only seven (2.2%) Veterans reported symptoms consistent with PTSD but did not meet criteria for CMI. However, 140 (43.9%) Veterans met criteria for CMI (5% severe CMI) but not did not report symptoms consistent with PTSD (**Figure 1**).

Relationship of Chronic Multisymptom Illness to Predeployment Symptoms

Of the Veterans who provided responses at 1 yr postdeployment, at predeployment 162 (50.9%) reported minimal physical symptom severity, 112 (35%) reported low physical symptom severity, 38 (11%) reported medium physical symptom severity, and 6 (1%) reported high physical symptom severity.

Chi-square analyses showed that soldiers who reported greater symptom severity at predeployment were more likely to report physical symptoms consistent with CMI 1 yr postdeployment (X^2 = 17.84, p = 0.01; **Table 2**). All of the soldiers who reported high symptom severity at baseline also met criteria for CMI at 1 yr postdeployment. Importantly, 150 (47%) soldiers who reported minimal symptom severity (i.e., the lowest category) at baseline also reported physical symptoms consistent with CMI at 1 yr postdeployment.

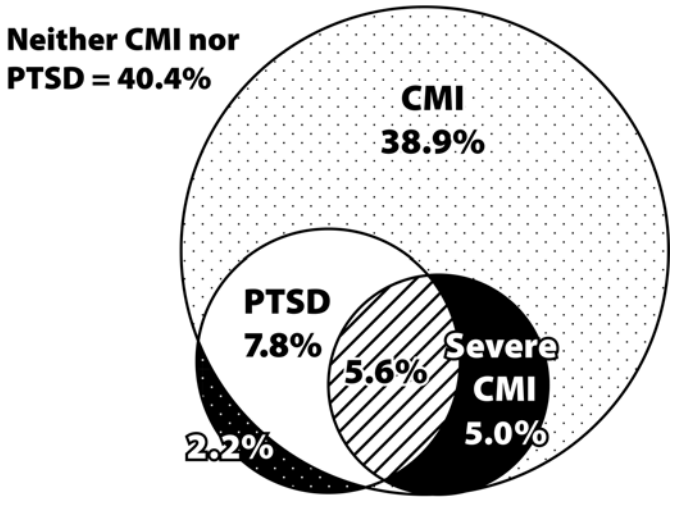

Figure 1.
Frequency of chronic multisymptom illness (CMI) and posttraumatic stress disorder (PTSD) among Operation Iraqi Freedom/Operation Enduring Freedom soldiers 1 yr after deployment.

Table 2.
Predeployment physical symptom severity and chronic multisymptom illness (CMI) status 1 yr after deployment, *n* (%).

Baseline Physical Symptom Severity	No CMI	Mild to Moderate CMI	Severe CMI
Minimal	85 (52.5)	64 (39.5)	13 (8.0)
Low	40 (35.4)	59 (52.2)	13 (12.4)
Medium	11 (28.9)	22 (57.9)	5 (13.2)
High	0 (0)	4 (66.7)	2 (33.3)

Relationship of Chronic Multisymptom Illness to Physical and Mental Health Function

Figure 2 depicts mental and physical health function at 1 yr postdeployment for Veterans who did not screen positive for CMI, Veterans who screened positive for mild to moderate CMI, and Veterans who screened positive for severe CMI. For reference, a 2 to 3 point difference on one of the subscales of the VR-36 is generally considered clinically significant. For each subscale, Veterans who screened positive for severe CMI reported functioning 10 points or more lower than that in soldiers who did not screen positive for CMI.

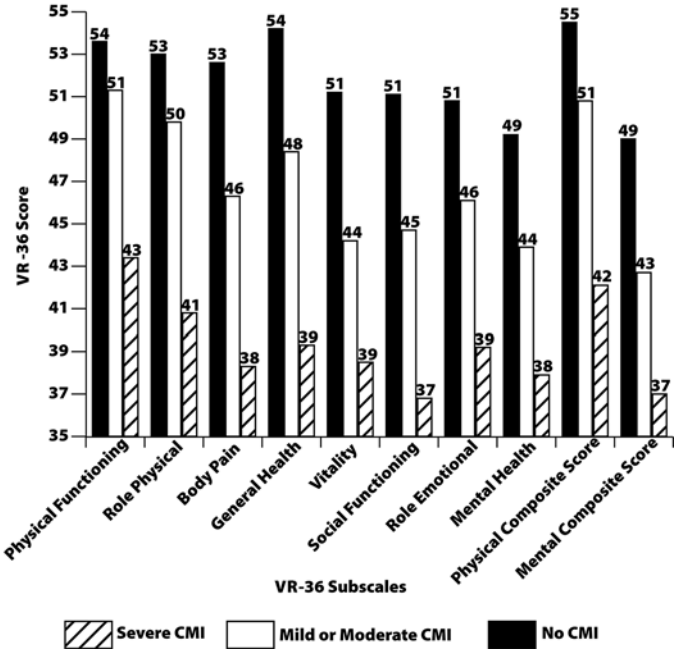

Figure 2.
Physical and mental health function subscales of Veterans RAND 36-Item Health Survey (VR-36) at 1 yr postdeployment for soldiers with no chronic multisymptom illness (CMI), mild to moderate CMI, and severe CMI. Higher scores (*y*-axis) indicate better functioning.

Two ANCOVAs were used to determine the relationship of CMI (no CMI, mild to moderate CMI, and severe CMI) to composite scores of mental (**Table 3**) and physical health function (**Table 4**). CMI was strongly related to physical health function 1 yr after deployment after controlling for predeployment levels of physical health function and physical symptoms, and for PTSD symptoms at 1 yr after deployment. CMI and mental health function were not significantly associated after controlling for predeployment levels of mental health function and physical symptoms, and PTSD symptoms at 1 yr postdeployment.

DISCUSSION

Chronic pain is a significant problem for OIF/OEF Veterans. For some OIF/OEF Veterans, this chronic pain may be part of a larger multisystem condition, termed CMI. Using a prospective longitudinal study of OIF/OEF soldiers, we found that 49.5 percent of OIF/OEF Veterans met criteria for mild to moderate CMI at 1 yr after deployment, and 10.8 percent met criteria for severe CMI. Almost all Veterans with chronic musculoskeletal pain also met criteria for CMI (90%). In this study, neither mild to moderate nor severe CMI were completely accounted for by PTSD or by predeployment levels of physical symptom severity. Further, Veterans who met criteria for either mild to moderate or severe CMI also reported clinically and statistically significantly worse physical health function than soldiers without CMI, even after controlling for predeployment physical health function and physical symptoms and PTSD symptoms at 1 yr postdeployment. To put this in perspective, on average, soldiers with severe CMI had physical health function almost as low as civilians with chronic illness [32].

Our results suggest that for some, if not many, OIF/OEF Veterans with chronic musculoskeletal pain, their chronic pain may be part of a larger CMI. This has implications for pain management or treatment. Providers should consider asking about and addressing the other chronic symptoms of OIF/OEF Veterans. Prior research has found that when providers' and patients' views on illnesses are nonconcordant, the patient is less adherent to treatment recommendations and less satisfied with the care [33]. For Veterans with chronic pain, treatments focused

Table 3.
Analysis of covariance predicting physical health function 1 yr after deployment (adjusted $R^2 = 0.25$).

	Mean Square	*F*	*p*-Value
Sex	0.44	0.01	0.93
Age	431.50	7.55	0.01
Predeployment Physical Functioning	1,113.12	19.47	0.00
Predeployment Physical Symptoms	0.57	0.01	0.92
PTSD symptoms 1 yr After Deployment	654.40	11.45	<0.001
CMI 1 yr After Deployment	587.65	10.28	<0.001

CMI = chronic multisymptom illness, PTSD = posttraumatic stress disorder.

Table 4.
Analysis of covariance predicting mental health function 1 yr after deployment (adjusted $R^2 = 0.48$).

	Mean Square	*F*	*p*-Value
Sex	170.41	2.14	0.14
Age	114.73	1.44	0.23
Predeployment Mental Health Functioning	1,392.74	17.50	0.00
Predeployment Physical Symptoms	129.89	1.63	0.20
PTSD Symptoms 1 yr After Deployment	13,464.31	169.16	<0.001
CMI 1 yr After Deployment	155.75	1.96	0.14

CMI = chronic multisymptom illness, PTSD = posttraumatic stress disorder.

on chronic pain that ignore the Veterans' fatigue or cognitive dysfunction may lead to poorer adherence and satisfaction. Management for Veterans with CMI may require going beyond traditional pain management approaches. For example, cognitive behavioral therapy is a recommended treatment for chronic pain. However, there likely needs to be greater tailoring of cognitive behavioral therapy to the specific needs of Veterans with CMI [34]. This may include treatment to improve sleep, scheduling of pleasant activities around episodes of fatigue, and cognitive remediation treatment.

After the Persian Gulf war, there was a prominent focus on CMI (called Gulf War Illness), the associated poor functioning [7], and the possible overlap of this condition with PTSD symptoms [16]. In contrast, the clinical focus for OIF/OEF Veterans has been on multiple diagnoses, each of which can be associated with significant physical symptoms, including chronic pain, PTSD, mTBI, depression, and polysubstance abuse [16,35–37]. Our study was limited in that we only assessed PTSD and pain symptoms and did not have measures of these other common postdeployment health conditions. However, it seems unlikely that unmeasured depression, mTBI, and substance abuse can fully account for the physical symptoms observed here. First, depression and substance abuse frequently co-occur with CMI but in prior studies have not been demonstrated to account for the symptoms of CMI (for a review see Burton [38]). Second, another possible candidate for the cause of CMI symptoms, mTBI, also appears unlikely to fully explain the extent of CMI. mTBI is thought to affect approximately 15 percent of OIF/OEF Veterans and commonly co-occurs with PTSD, yet we found that 43 percent of OIF/OEF Veterans met criteria for CMI and did not meet criteria for PTSD. Thus, even if mTBI had no overlap with PTSD, there would still be an estimated 28 percent of our sample that met criteria for CMI but not for either PTSD or mTBI (i.e., 43% minus 15%). Future studies should measure the full range of possible comorbidities to better understand the relationship of CMI to each of these other postdeployment conditions.

There are several limitations of this study. Although the CDC definition for CMI is recommended by the Institute of Medicine, it is not without limitations. Most critically, there are no exclusion criteria for the CDC definition, and thus conditions such as HIV, multiple sclerosis, and rheumatoid arthritis may explain these symptoms for some of our participants. The relatively short time frame between deployment and demonstration of CMI in this sample, however, suggests that the overlap with chronic conditions like these should not yet be very high. Second, this definition was developed based on

symptom presentations in Persian Gulf war Veterans. The symptoms we found to be most common were not necessarily those most commonly reported after the Persian Gulf war, suggesting that there may be a unique case definition of CMI for OIF/OEF Veterans that takes into account deployment-related factors that differ for these deployments. Other limitations include that we did not have a complete assessment of CMI symptoms predeployment, and thus had to rely on the PHQ-15–based measure of physical symptom severity at predeployment. We also did not have a validated measure of chronic musculoskeletal pain. Finally, by using a self-report measure of CMI we are capturing the number of soldiers in our sample who have symptoms consistent with CMI. An interview with a provider is necessary to determine the best diagnosis.

CONCLUSIONS

To our knowledge, this is one of the first studies of CMI in OIF/OEF soldiers. Our data suggest that many OIF/OEF Veterans are experiencing multiple chronic symptoms that meet criteria for CMI. Further, meeting CMI criteria is associated with lower physical health function to an extent that is likely clinically significant. Finally, the prevalence of CMI in this sample is not fully accounted for by either predeployment physical symptoms or PTSD. Because we did not use a diagnostic interview with a clinician, we do not know the best diagnosis for participants in this sample. However, our results suggest that clinicians should consider CMI when assessing OIF/OEF Veterans with postdeployment health concerns. This includes considering broader treatment strategies that encompass both pain management as well as attention to other bothersome symptoms such as fatigue, trouble sleeping, or cognitive symptoms.

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Analysis and interpretation of data: L. M. McAndrew.
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Prevalence and correlates of painful conditions and multimorbidity in national sample of overweight/obese Veterans

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Abstract—Chronic pain and overweight/obesity are prevalent public health concerns and occur at particularly high rates among Veterans. This study examined the prevalence and correlates of two common painful conditions (back pain and arthritis/joint pain) among overweight/obese Veterans in Veterans Health Administration (VHA) care. Participants (N = 45,477) completed the MOVE!23, a survey intended to tailor treatment for Veterans in VHA's MOVE! weight-management program. Overall, 72% of the sample reported painful conditions, with 10% reporting back pain, 26% reporting arthritis/joint pain, and 35% reporting both. We used multinomial logistic regression with "no pain" as the reference category to examine the association between painful conditions and participant characteristics. After multivariable adjustment, female Veterans had higher odds of reporting arthritis/joint pain and combined back and arthritis/joint pain than no pain. Participants with higher body mass index had higher odds of reporting arthritis/joint pain and both back and arthritis/joint pain. The likelihood of painful conditions was higher in Veterans with comorbidities (hypertension, hyperlipidemia, lung disease, depression, anxiety, or posttraumatic stress disorder) and generally increased with the number of comorbidities reported (i.e., 5 or more). Overweight/obese Veterans frequently report painful conditions and, among those with pain, often have multiple comorbidities. These factors may increase the complexity of clinical management and necessitate refinements to weight-management programs.

Key words: arthritis, back pain, BMI, chronic pain, comorbidities, multimorbidity, obesity, overweight, Veterans, weight management.

INTRODUCTION

Pain and obesity are two of the most prevalent chronic diseases in the United States [1–3] and are especially common among Veterans treated within the Veterans Health Administration (VHA) [4–6]. Recent estimates of the prevalence of overweight/obesity are 68.0 percent for the general U.S. population [1] and 76.9 percent for Veterans within VHA [7]. Veterans also have higher waist circumferences than the general population [8]. While limited epidemiological data regarding pain is a recognized barrier to determining the prevalence of chronic pain in the United States [9], in the report, "Relieving pain in America: A blueprint for transforming prevention, care, education and research," the Institute of Medicine notes that approximately 100 million Americans experience chronic pain [9]. Recently, chronic pain in the general population, as

Abbreviations: BMI = body mass index, CAD = coronary artery disease, CI = confidence interval, HTN = hypertension, OR = odds ratio, PTSD = posttraumatic stress disorder, VA = Department of Veterans Affairs, VHA = Veterans Health Administration.

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reported by national surveys, has been found to range from 19 [10] to 43 percent [11] among age, race/ethnicity, and/or sex standardized national samples. The prevalence of chronic pain among Veterans appears to be comparable to or higher than non-Veterans, with one study showing a significantly higher rate of low back pain among Veterans compared with non-Veterans (44% vs 25%, respectively) in primary care settings [2].

Similar to reported rates of overweight/obesity and chronic pain alone, rates of comorbid pain and overweight/obesity are also high, with some estimates ranging from 20 to 45 percent of overweight/obese individuals reporting pain [12]. Recent data from the 2010 National Health Interview Survey demonstrated that among those with persistent pain (i.e., a duration of ≥3 mo) in the general U.S. population, 18.2 percent are overweight and 25.3 percent are obese [10]. Higher body mass index (BMI) was associated with increased risk of recent pain [13] and report of a painful condition within the previous year [12]. Further, obesity has been shown to predict the onset and progression of pain [14], and obese patients have reported engaging in poor eating habits and avoiding physical activity in response to pain [15].

The high rate of comorbidity between pain and overweight/obesity has implications for the treatment of both conditions. Patients commonly endorse pain as a barrier to weight loss [15–16], and obesity has been shown to moderate the impact of treatment for chronic pain self-management in Veterans in VHA care [17]. There is some evidence supporting integrated interventions targeting both weight loss and improvement in physical functioning, though they tend to focus specifically on intensive interventions for patients with a narrowly defined type of painful condition, such as knee osteoarthritis [18–19].

More broadly, information regarding correlates of both pain and obesity is limited [20], particularly among Veterans receiving VHA care. There is a wealth of data describing high-prevalence, high-impact multimorbidity among Veterans in general [21–23]. There is also a wealth of data describing comorbidities among Veterans with overweight/obesity, such as hypertension (HTN), type 2 diabetes, hypercholesterolemia, and heart disease [7,24], as well as alcohol and drug use disorders, depression, and posttraumatic stress disorder (PTSD) [24]. The same is true for correlates of pain and painful conditions among Veterans, including overweight/obesity, anxiety disorders, PTSD, mood disorders, and substance use disorders [25–26]. There is emerging evidence that pain interferes with the management of other chronic conditions, such as diabetes [27–28], and leads to poorer outcomes for both comorbid conditions, further suggesting a need to examine comorbid pain and obesity. Better management of both pain and overweight/obesity may lead to improved outcomes in both conditions.

Given the high prevalence of pain and overweight/obesity among Veterans, as well as evidence suggesting that each may serve as a barrier to treatment of the other, further investigation is warranted to better understand the clinical correlates of Veterans with comorbid pain and overweight/obesity. The association between pain and overweight/obesity may have important implications for the potential refinement of weight-management programs, such as the VHA's national program, MOVE!. The objective of the current paper is to examine the prevalence and correlates of self-reported painful conditions, specifically arthritis/joint pain and back pain, among overweight/obese Veterans expressing interest in weight-management treatment.

METHODS

Participants

The national sample consisted of 45,477 overweight/obese Veterans who received healthcare in VHA facilities and expressed interest in weight management. Veterans in this sample had a self-reported weight and height consistent with a BMI ≥25 and completed the MOVE!23 survey in 2006. Survey data were collected during routine primary care screening from patients who expressed interest in the MOVE! weight-management program. However, not all patients who indicated interest and completed the MOVE!23 ultimately enrolled or participated in the MOVE! program.

Data Source

A secondary analysis of cross-sectional data collected using the MOVE!23 survey was conducted. The MOVE!23 was developed by VHA in conjunction with the VHA's National Center for Health Promotion and Disease Prevention as a clinical tool to assist providers in working with Veterans to achieve weight loss and improvement in related comorbid conditions. The survey contains 23 questions that assess demographics, weight history, medical and psychiatric comorbidities (including painful conditions), eating habits, exercise, and motivation and support

[29]. The MOVE!23 survey was developed to aid in tailoring treatment for patients in the VHA's national MOVE! weight-management program.

While the measure as a whole does not have published psychometric properties, sections of the MOVE!23 have been validated (e.g., perceived barriers and contributors to weight gain [25]).The MOVE!23 is inherently face valid, and the choice of items for inclusion in the current study included those questions that contained information about pain (i.e., painful conditions), self-reported demographics, and self-reported medical and mental health comorbidities to include in the analyses as covariates.

Study Variables

Demographics

Survey respondents reported their sex, age, and race/ethnicity.

Overweight/Obesity

BMI was calculated using self-reported height (inches) and weight (pounds). BMI was categorized as: overweight (BMI 25.0 to 29.9 kg/m^2), class I obesity (BMI 30.0 to 34.9 kg/m^2), class II obesity (BMI 35.0 to 39.9 kg/m^2), and class III obesity (BMI ≥40.0 kg/m^2) [30].

Comorbidities

All medical and mental health comorbidities and related problems, as well as painful conditions, were derived from a single item on the MOVE!23 survey: "Please indicate any of the following that apply to you." There were 20 possible responses for medical comorbidities and acute and chronic medical conditions and problems and 13 possible responses for mental health comorbidities and related problems.

Medical comorbidities. Respondents reported past or current medical conditions, including diabetes, HTN, heart disease (coronary artery disease [CAD]), high blood cholesterol (hyperlipidemia), and lung disease (i.e., emphysema, chronic obstructive pulmonary disease, asthma). These 5 comorbidities, of the 20 possible responses, were targeted for examination for the current study because they are high-impact, high-prevalence chronic conditions among Veterans. These have also been highlighted in previous studies as comorbidities of overweight/obesity and/or painful conditions among Veterans [7,24]. We excluded assessed conditions that did not represent actual diagnoses (e.g., loss of balance because of dizziness or passing out, chest pains not previously evaluated by your doctor, shortness of breath at rest, amputation, someone in your immediate family with heart problems at an age <50 yr, and poor circulation in the legs), those that were acute problems (e.g., active infection of any kind or any chronic medical problem that has recently been out-of-control, unstable, or flared up), those with low prevalence compared with other conditions among Veterans (e.g., hernia, retinal bleeding, spinal cord injury, osteoporosis, or bone disease), and those that were nonspecific (i.e., combined several conditions, symptoms, or procedures, such as stroke, transient ischemic attack, or carotid surgery in the neck).

Mental health comorbidities. Respondents reported past or current mental health conditions and other problems: depression, tobacco use/smoking, substance abuse or dependence, anxiety problems or nervousness, PTSD, bipolar disorder, schizophrenia, and obsessive compulsive disorder. These 8 mental health comorbidities, of the 12 possible responses, were targeted for examination for the current study because they are not only high-impact, high-prevalence mental health conditions among Veterans they are also comorbidities of overweight/obesity and/or painful conditions among Veterans [24–26]. The remaining conditions do not represent diagnoses and are too general to enhance the understanding of the population (e.g., general unhappiness, too much stress, and family or relationship problems) or are nonspecific (i.e., eating disorder).

Pain Groups

Participants were categorized into the following pain groups: no pain (i.e., neither back pain nor arthritis/joint pain), back pain only, arthritis/joint pain only, and combined back and arthritis/joint pain (i.e., those respondents who endorsed *both* pain problems) based on their endorsement of the "back pain or spinal disc disease" and "arthritis or joint pain" responses for the comorbidities item described previously.

Analyses

Descriptive statistics for demographic and clinical variables are presented by pain group and overall. Because the outcome pain group is a nominal categorical variable with 4 levels, we used a multinomial logistic regression model with the "no pain" (i.e., no "painful

conditions") group as the reference category to simultaneously investigate the correlates of belonging to this group instead of the other three groups. Specifically, this model compares the probability of being in the "back pain only," "arthritis/joint pain only," or "both back and arthritis/joint pain" groups relative to the "no pain" group and relates these comparisons to the following subject demographic and clinical characteristics: sex, age (categorical variable with categories 21–34, 35–44, 45–54, 55–64, 65–74, and ≥75 yr), race/ethnicity (White, Black/African American, Hispanic, or Other), BMI class (overweight and obese class I, II, or III), and the medical and mental comorbidities described previously (each categorized as present/absent). We present the adjusted odds ratios (ORs) from the multinomial logistic regression model as a measure of association between pain group and subject characteristics. To investigate the association between number of comorbidities and pain group, we fit an additional multinomial logit model including as predictors number of comorbidities (categorical variable with values 0, 1, 2, 3, 4, and ≥5), age, sex, race/ethnicity, and BMI class.

We performed multiple imputation to avoid potentially biasing the results by excluding subjects with missing race/ethnicity (16%) from the analysis. This method assumes that the data are "missing at random"; i.e., that the probability of missingness depends only on observed data. We generated 10 complete data sets via predictive mean matching imputation (as implemented by the "aregImpute" function within the "Hmisc" package in the statistical software R [R Foundation; Vienna, Austria]), separately analyzed each data set by fitting a multinomial logistic regression model, and then combined results across data sets by using Rubin's rules. The imputed results are reported in this article. Because our sample was large and statistically significant differences may not reflect clinically significant findings, we focus on results that were high in magnitude in terms of ORs (i.e., significantly greater or less than 1.0) and also statistically significant at the 0.05 level.

RESULTS

Of the 45,477 subjects in our sample, 28 percent of participants reported "no pain" (i.e., no back or arthritis/joint pain), 10 percent reported "back pain" only, 26 percent reported "arthritis/joint pain" only, and 35 percent reported "both back and arthritis/joint pain." **Table 1** contains the characteristics of the sample by pain group and overall. Subjects were mostly male (86.6%) and had a mean ± standard deviation (SD) age of 57.3 ± 11.4. Subjects in the "back pain only" group were slightly younger than the rest, and those in the three painful conditions groups were more likely to be in higher BMI categories than those in the "no pain" group. Overall, the most commonly reported medical comorbidities were HTN (62.5%), hyperlipidemia (47.7%), and diabetes (36.5%), which were all less likely to be reported by the "no pain" group than the other three groups. Depression (36.4%), anxiety (30.0%), and PTSD (21.1%) were the most prevalent mental health comorbidities and were less common in the "no pain" group than in the other groups. The mean number of comorbidities in the overall sample was 3.0 ± 2.0 and was lower on average in the "no pain" group than in the other groups. Veterans in the "both back and arthritis/joint pain" group were most likely to report ≥5 comorbidities, with 32.3 percent of the back and arthritis/joint pain group reporting ≥5 comorbidities.

Table 2 contains the results obtained from multinomial logistic regression after imputing the missing race/ethnicity data. For each predictor, the table gives estimates of the adjusted ORs of being in each of the three pain groups (the back pain only, arthritis/joint pain only, or both) instead of the reference no pain group and associated 95 percent confidence intervals (CIs).

After controlling for the other predictors in the model, male Veterans had lower odds of reporting "arthritis/joint pain only" (OR = 0.76; 95% CI 0.70 to 0.83) and "both back and arthritis/joint pain" (OR = 0.75; 95% CI 0.69 to 0.81) than "no pain" compared with female Veterans. Older Veterans (≥35 yr) were more likely than younger ones (reference 21–34 yr) to report "arthritis/joint pain only" and "both back and arthritis/joint pain" than "no pain" and less likely to report "back pain only" than "no pain." The estimated odds of being in the "arthritis/joint pain only" and "both back and arthritis/joint pain" groups versus the "no pain" group increased with increasing BMI class.

Participants who endorsed HTN, CAD, or lung disease had higher odds than participants without those conditions of being in the three painful conditions groups instead of the "no pain" group (all corresponding OR significantly >1). Similarly, participants with depression, anxiety, or PTSD were more likely than those without those conditions to be in any of the three painful conditions groups (OR significantly >1). Those who reported

Table 1.
Descriptive statistics by pain group and overall (percent/frequency).

Variable	No Pain *N* = 12,812 (28%)	Back Pain Only *N* = 4,766 (10%)	Arthritis/Joint Pain Only *N* = 11,790 (26%)	Both Back & Arthritis/Joint Pain *N* = 16,109 (35%)	Overall *N* = 45,477 (100%)
Male	87.8 (11,243)	85.1 (4,058)	87.7 (10,337)	85.3 (13,746)	86.6 (39,384)
Age, yr (mean ± SD)	57.1 ± 12.2	54.0 ± 12.1	59.3 ± 11.0	57.0 ± 10.6	57.3 ± 11.4
Age Category					
21–34	5.0 (637)	7.5 (358)	2.5 (300)	2.8 (446)	3.8 (1,741)
35–44	10.4 (1,334)	13.6 (648)	7.1 (840)	9.0 (1,445)	9.4 (4,267)
45–54	19.9 (2,544)	24.0 (1,144)	17.6 (2,074)	23.5 (3,791)	21.0 (9,553)
55–64	38.9 (4,983)	38.3 (1,825)	43.6 (5,136)	44.5 (7,170)	42.0 (19,114)
65–74	19.2 (2,464)	12.6 (599)	21.2 (2,494)	15.3 (2,462)	17.6 (8,019)
≥75	6.6 (850)	4.0 (192)	8.0 (946)	4.9 (795)	6.1 (2,783)
Ethnicity/Race					
White	57.0 (7,308)	54.9 (2,617)	59.6 (7,032)	60.1 (9,678)	58.6 (26,635)
Black/African American	16.3 (2,093)	18.1 (865)	16.0 (1,883)	14.7 (2,367)	15.8 (7,208)
Hispanic	7.4 (949)	8.4 (402)	6.4 (751)	6.3 (1,016)	6.9 (3,118)
Other	2.1 (266)	2.6 (126)	2.5 (299)	3.1 (503)	2.6 (1,194)
Declined to Report	17.1 (2,196)	15.9 (756)	15.5 (1,825)	15.8 (2,545)	16.1 (7,322)
BMI, median (IQR)	34.6 (31.4–39.1)	35.4 (31.8–39.9)	36.0 (32.2–40.9)	36.5 (32.6–41.7)	35.7 (32.1–40.6)
BMI Class					
Overweight	14.9 (1,906)	13.6 (648)	11.3 (1,332)	10.1 (1,620)	12.1 (5,506)
Obese Class I	38.2 (4,900)	33.6 (1,599)	32.6 (3,842)	30.6 (4,930)	33.6 (15,271)
Obese Class II	25.3 (3,242)	28.4 (1,352)	27.6 (3,249)	27.4 (4,408)	26.9 (12,251)
Obese Class III	21.6 (2,764)	24.5 (1,167)	28.6 (3,367)	32.0 (5,151)	27.4 (12,449)
Comorbidities					
HTN	55.1 (7,054)	58.4 (2,781)	65.5 (7,728)	67.3 (10,838)	62.5 (28,401)
Diabetes	32.6 (4,178)	33.8 (1,610)	39.2 (4,621)	38.5 (6,210)	36.5 (16,619)
CAD	18.8 (2,409)	21.2 (1,010)	25.0 (2,949)	28.0 (4,506)	23.9 (10,874)
Hyperlipidemia	41.9 (5,370)	44.8 (2,135)	48.2 (5,688)	52.8 (8,513)	47.7 (21,706)
Lung Disease	8.6 (1,098)	12.6 (600)	13.9 (1,641)	20.2 (3,253)	14.5 (6,592)
Tobacco Use/Smoking	13.3 (1,699)	18.4 (877)	12.7 (1,503)	16.9 (2,730)	15.0 (6,809)
Substance Use	2.5 (326)	3.8 (181)	2.7 (319)	3.8 (606)	3.1 (1,432)
Depression	23.1 (2,965)	39.5 (1,884)	31.5 (3,716)	49.5 (7,969)	36.4 (16,534)
Anxiety	18.7 (2,401)	31.8 (1,515)	26.0 (3,071)	41.2 (6,639)	30.0 (13,626)
PTSD	13.3 (1,702)	22.5 (1,073)	18.2 (2,143)	29.2 (4,698)	21.1 (9,616)
Bipolar Disorder	4.5 (582)	6.7 (318)	4.3 (512)	7.8 (1,249)	5.9 (2,661)
Schizophrenia	3.3 (420)	2.6 (125)	2.0 (240)	2.7 (429)	2.7 (1,214)
OCD	3.3 (420)	5.2 (246)	4.4 (520)	7.7 (1,242)	5.3 (2,428)
No. Comorbidities					
0	12.7 (1,629)	9.0 (429)	8.1 (957)	4.7 (760)	8.3 (3,775)
1	21.7 (2,774)	15.5 (740)	15.7 (1,850)	10.6 (1,713)	15.6 (7,077)
2	22.8 (2,925)	19.1 (912)	20.7 (2,437)	15.6 (2,506)	19.3 (8,780)
3	19.7 (2,526)	18.9 (899)	20.4 (2,406)	18.9 (3,052)	19.5 (8,883)
4	11.7 (1,498)	15.4 (736)	15.8 (1,860)	17.8 (2,874)	15.3 (6,968)
≥5	11.4 (1,460)	22.0 (1,050)	19.3 (2,280)	32.3 (5,204)	22.0 (9,994)
Mean ± SD	2.4 ± 1.7	3.0 ± 2.0	2.9 ± 1.9	3.7 ± 2.1	3.0 ± 2.0

Note: all *p*-values for whether there are differences among 4 groups with respect to variables reported are < 0.001.
BMI = body mass index, CAD = coronary artery disease, HTN = hypertension, IQR = interquartile range, No. = number, OCD = obsessive compulsive disorder, PTSD = posttraumatic stress disorder, SD = standard deviation.

Table 2.
Adjusted odds ratio (OR) estimates from multivariable multinomial logistic model fit on $N = 45,477$ subjects (imputed results).

Characteristic	"Back Pain Only" vs "No Pain"			"Arthritis/Joint Pain Only" vs "No Pain"			"Both Back & Arthritis/ Joint Pain" vs "No Pain"		
	OR	95% Wald CI		OR	95% Wald CI		OR	95% Wald CI	
		Lower Limit	Upper Limit		Lower Limit	Upper Limit		Lower Limit	Upper Limit
Male (vs female)	0.99	0.89	1.10	0.76*	0.70	0.83	0.75*	0.69	0.81
Age Category									
21–34 (ref)									
35–44	0.83*	0.70	0.97	1.25*	1.06	1.47	1.39*	1.20	1.61
45–54	0.73*	0.63	0.85	1.56*	1.34	1.82	1.78*	1.54	2.04
55–64	0.56*	0.48	0.66	1.93*	1.66	2.24	1.59*	1.39	1.83
65–74	0.45*	0.38	0.53	2.20*	1.88	2.58	1.57*	1.36	1.83
≥75	0.44*	0.35	0.55	2.65*	2.22	3.16	1.69*	1.42	2.00
Ethnicity/Race									
White (ref)									
Black/African American	1.04	0.95	1.13	1.07	1.00	1.14	0.88*	0.82	0.94
Hispanic	1.03	0.91	1.17	0.92	0.83	1.02	0.79*	0.72	0.87
Other	1.12	0.92	1.38	1.20*	1.02	1.42	1.25*	1.07	1.47
BMI Class									
Overweight (ref)									
Obese Class I	0.90	0.81	1.01	1.13*	1.04	1.22	1.14*	1.05	1.24
Obese Class II	1.10	0.99	1.24	1.43*	1.31	1.56	1.47*	1.35	1.60
Obese Class III	1.06	0.95	1.20	1.73*	1.58	1.89	1.91*	1.75	2.08
Comorbidities (presence vs absence)									
HTN	1.18*	1.09	1.27	1.29*	1.21	1.36	1.37*	1.30	1.45
Diabetes	1.04	0.96	1.13	1.04	0.98	1.10	0.96	0.91	1.01
CAD	1.23*	1.12	1.34	1.17*	1.10	1.25	1.37*	1.28	1.45
Hyperlipidemia	1.07	0.99	1.15	1.07*	1.02	1.13	1.23*	1.17	1.30
Lung Disease	1.40*	1.25	1.56	1.47*	1.35	1.60	2.02*	1.87	2.19
Tobacco Use/Smoking	1.23*	1.12	1.35	1.01	0.94	1.10	1.13*	1.05	1.22
Substance Use	1.05	0.86	1.27	1.03	0.88	1.22	1.01	0.87	1.17
Depression	1.58*	1.46	1.72	1.33*	1.25	1.43	2.02*	1.90	2.15
Anxiety	1.40*	1.29	1.53	1.36*	1.27	1.46	1.83*	1.71	1.95
PTSD	1.31*	1.19	1.44	1.18*	1.10	1.28	1.53*	1.43	1.64
Bipolar Disorder	0.97	0.83	1.12	0.82*	0.72	0.94	0.92	0.82	1.04
Schizophrenia	0.51*	0.41	0.63	0.56*	0.47	0.66	0.47*	0.40	0.54
OCD	1.01	0.85	1.20	1.13	0.98	1.30	1.26*	1.12	1.43

Note: Model used pain group (with categories "back pain only," "arthritis/joint pain only," and "both back and arthritis/joint pain" vs reference category "no pain") as an outcome and simultaneously adjusted for all predictors listed in table.
*$p \leq 0.05$.
BMI = body mass index, CAD = coronary artery disease, CI = confidence interval, HTN = hypertension, OCD = obsessive compulsive disorder, PTSD = posttraumatic stress disorder, ref = reference.

schizophrenia had markedly higher odds than those without schizophrenia to report being in the reference "no pain" group relative to the other three groups.

Table 3 presents adjusted OR estimates for the association between number of comorbidities and pain group. A higher number of comorbidities was generally associated with higher odds of being in the three groups with pain rather than in the "no pain" group. Notably, those reporting ≥5 comorbidities were substantially more likely to be in the "back pain only" group (adjusted OR 3.00,

Table 3.
Adjusted odds ratio (OR) estimates for number of comorbidities from multivariable multinomial logistic model fit on N = 45,477 subjects (imputed results).

No. Comorbidities (vs 0)	"Back Pain Only" vs "No Pain"			"Arthritis/Joint Pain Only" vs "No Pain"			"Both Back & Arthritis/Joint Pain" vs "No Pain"		
	OR	95% Wald CI		OR	95% Wald CI		OR	95% Wald CI	
		Lower Limit	Upper Limit		Lower Limit	Upper Limit		Lower Limit	Upper Limit
1	1.09	0.95	1.24	1.07	0.97	1.18	1.31*	1.18	1.46
2	1.33*	1.16	1.51	1.30*	1.18	1.43	1.80*	1.62	1.99
3	1.54*	1.34	1.75	1.45*	1.32	1.60	2.51*	2.27	2.78
4	2.11*	1.83	2.43	1.87*	1.68	2.08	3.89*	3.49	4.33
≥5	3.00*	2.62	3.44	2.38*	2.14	2.65	7.07*	6.36	7.86

Note: Model used pain group (with categories "back pain only," "arthritis/joint pain only," and "both back and arthritis/joint pain" vs reference category "no pain") as an outcome and adjusted for number of comorbidities, sex, age, ethnicity/race, and body mass index class.
*$p \leq 0.05$.
CI = confidence interval, No. = number.

95% CI 2.62 to 3.44), "arthritis/joint pain only" group (adjusted OR 2.38, 95% CI 2.14 to 2.65), or "both back and arthritis/joint pain" group (adjusted OR 7.07, 95% CI 6.36 to 7.86) than in the "no pain" group.

DISCUSSION

A very high proportion of the sample (72%) of overweight/obese Veterans reported ≥1 painful condition, with 10 percent reporting back pain only, 26 percent reporting arthritis/joint pain only, and 35 percent reporting combined back and arthritis/joint pain. Participants with higher BMIs were more likely to report painful conditions (i.e., arthritis/joint pain or both back and arthritis/joint pain). Among Veterans with combined back and arthritis/joint pain, the proportion with any given comorbid condition was quite high (e.g., 67.3% HTN, 38.5% diabetes, 52.8% hyperlipidemia, 20.2% lung disease, 49.5% depression, and 41.2% anxiety), and those patients were most likely to report ≥5 comorbidities (32.3%). Given the emerging evidence that pain interferes with the self-management of other conditions or is associated with poorer outcomes (e.g., diabetes, PTSD), it may be helpful to examine the role of pain in weight-management outcomes and potentially address pain in weight-management programs such as MOVE! [28].

The literature on comorbid pain and overweight/obesity shows that patients frequently endorse pain as a barrier to weight loss [15–16]. Given that this study examined a large sample of Veterans with overweight/obesity who were interested in weight management, the finding that the vast majority are experiencing painful conditions is likely to have an effect on the success of traditional weight-management programs, such as the VHA's MOVE! program, which encourage physical activity. Weight loss programs such as MOVE! may need to be modified to address pain management through the addition of pain education and behavioral pain self-management skills. For example, if patients are able to learn appropriate pain self-management skills, such as task persistence, pacing, and cognitive restructuring, pain may serve as less of a barrier to increasing physical activity, thus theoretically improving weight loss outcomes.

One compelling feature of the data presented in the current study is that Veterans who are interested in MOVE! have an extremely high burden of comorbidity, particularly those with >1 painful condition (i.e., the Veterans reporting ≥5 comorbidities were most likely to report 2 painful conditions). This is a possible explanation for the low mean weight loss seen in the MOVE! program [31]. Although MOVE! was designed on a population health approach and was developed to be a low barrier to entry program that would attract as many Veterans as possible, the patients who attend have multimorbidities, including extremely high rates of painful conditions, that likely complicate care and interfere with their weight loss efforts. Efforts to adapt MOVE! for Veterans with complex psychiatric illnesses may provide a model for how to do this for Veterans with comorbid pain conditions [32].

Generally, patients with medical and mental health conditions were more likely than those without the conditions to report being in each of the three groups with pain

(the back pain only, arthritis/joint pain only, and both back and arthritis/joint pain groups) rather than in the group without pain. In particular, they had the highest adjusted odds of being in the combined back and arthritis/joint pain group. This is consistent with recent Veteran data demonstrating that those with persistent pain were more likely to report comorbid conditions, including diagnoses of mood disorders, PTSD, substance use disorders, anxiety disorders, and traumatic brain injury; they were also more likely to have a BMI consistent with overweight/obesity [33]. Other research has shown that those with multiple painful conditions have a number of additional medical and mental health comorbidities, along with higher burden of illness and cost of care [34]. Properly addressing chronic pain in medically complex patients may improve health status, functioning, and quality of life, in addition to improving other health conditions [28].

A previous study of Operation Iraqi Freedom/Operation Enduring Freedom Veterans showed sex differences in the prevalence and severity of pain [26]. Similarly, female Veterans in the current study were more likely to report arthritis/joint pain and combined back and arthritis/joint pain than male Veterans. Despite controlling for variables such as age, race, and BMI, all of which are typically associated with differences in reporting of pain and painful conditions, this difference between male and female Veterans persisted. Female Veterans with overweight/obesity may be especially vulnerable to less-than-desirable weight loss outcomes if pain is not addressed in the context of weight-management programs.

In the current study, patients with comorbid mental health conditions, including depression and PTSD, were more likely than those without the conditions to report being in the groups with pain (the back pain only, arthritis/joint pain only, and both back and arthritis/joint pain groups) relative to the "no pain" group, a finding that is consistent with existing data describing Veterans with chronic pain [33,35–38]. However, those patients reporting comorbid schizophrenia were less likely to report back pain or arthritis/joint pain. The limited literature on persistent pain in patients with schizophrenia is mixed. The results in the current study are consistent with an administrative data study of VHA patients with schizophrenia that found lower associations between schizophrenia and pain conditions than for those without a serious mental illness after controlling for demographic variables [39]. In contrast, another recent study found the prevalence and intensity of pain appears to be comparable between those with schizophrenia and those without, with the exception of more acute, severe pain such as headache following lumbar puncture, in which patients with schizophrenia are less likely to report pain [40].

Importantly, the current study included a large sample of nearly 46,000 patients. Given the sample size, it is not surprising that many of the associations were statistically significant. Because clinical meaningfulness is difficult to assess based on the OR, it may be helpful to consider covariate-adjusted absolute proportions ("recycled predictions"; **Table 4**) [41]. When considering the effect of BMI category, for example, these proportions allow us to compare the estimated distribution of the outcome across BMI categories while keeping constant all other covariates at the observed values. After adjusting for the other covariates, 31 percent of overweight patients reported "both back and arthritis/joint pain," whereas 40 percent of patients with class III obesity reported "both back and arthritis/joint pain." This is an absolute difference in proportions of 9 percent, which translates into a large number of patients reporting severe obesity and comorbid back and arthritis/joint pain.

The current study has several limitations. One significant limitation is that the MOVE!23 was the sole source of data; thus all data are self-reported (i.e., height, weight, and comorbidities) and obtained from a small proportion of Veterans who were interested in weight management among the estimated 73 percent of Veterans in VHA care with overweight/obesity [4]. More specifically, the MOVE!23 question from which data for painful conditions and comorbidities for the current study were derived does not specifically ask about "diagnosed" conditions. It simply asks patients to determine whether each condition applies to them. This limits the validity of the diagnoses reported in the results of the current study. In addition, given that our sample has a higher average BMI than is found in the population of Veterans in VHA care, it is not surprising that the high prevalence of comorbidity and pain reporting is greater than typically seen in the general Veteran population.

Because these data were limited to endorsement or nonendorsement of a painful condition, the magnitude of pain and pain-related functional interference was not assessed. This limits the generalizations about pain in this sample because there is no multidimensional assessment of pain variables, including the chronicity of pain. Further, the survey included questions about only common musculoskeletal pain conditions and did not assess other common painful conditions. Thus, it must be

Table 4.
Covariate-adjusted proportions in each pain group by subject characteristics ("recycled predictions" obtained from multinomial logit model in **Table 2**).

Variable	No Pain	Back Pain	Arthritis/ Joint Pain	Both Back & Arthritis/ Joint Pain
Sex				
Female	24	9	28	39
Male	28	11	26	35
Age Category				
21–34	34	21	18	28
35–44	31	16	19	34
45–54	27	12	22	38
55–64	28	9	27	36
65–74	27	7	31	34
≥75	25	7	33	35
Ethnicity/Race				
White	28	10	26	36
Black/African American	28	11	28	33
Hispanic	30	12	26	32
Other	23	10	27	40
BMI Class				
Overweight	33	13	24	31
Obese Class I	31	11	25	33
Obese Class II	26	11	27	36
Obese Class III	23	9	28	40
Comorbidities				
No HTN	31	11	25	33
HTN	26	10	27	37
No Diabetes	28	10	26	36
Diabetes	28	11	26	35
No CAD	29	11	26	35
CAD	25	10	26	39
No Hyperlipidemia	29	11	27	34
Hyperlipidemia	26	11	26	37
No Lung Disease	29	11	26	34
Lung Disease	20	10	25	45
No Tobacco Use/Smoking	28	10	26	35
Tobacco Use/Smoking	26	12	25	37
No Substance Use	28	11	26	36
Substance Use	27	11	27	35
No Depression	31	10	27	32
Depression	22	11	25	42
No Anxiety	30	11	27	33
Anxiety	22	11	26	42
No PTSD	29	11	27	34
PTSD	23	11	25	41
No Bipolar Disorder	28	10	26	36
Bipolar Disorder	31	11	23	35
No Schizophrenia	27	11	26	36
Schizophrenia	42	8	22	28
No OCD	28	11	26	35
OCD	25	10	26	39

BMI = body mass index, CAD = coronary artery disease, HTN = hypertension, OCD = obsessive compulsive disorder, PTSD = posttraumatic stress disorder.

assumed that some participants in the no pain group had other common pain conditions, such as neuropathy or headache. An interesting question is whether musculoskeletal conditions are particularly relevant in the context of management of weight problems. Future research could consider a broader array of painful conditions and examine questions about specificity of associations between pain and overweight/obesity. Finally, this study was cross-sectional and the directional nature of relationships examined in this study cannot be determined.

Identifying subgroups of the overweight/obese population (such as those with painful conditions) allows for future research to determine whether these groups can be adequately treated with existing services or whether modifications are needed to address chronic pain and prevalent pain-related comorbidities within the VHA's national weight-management program, MOVE!. Examining the association between painful conditions and overweight/obesity may assist with determining whether painful conditions add to the complexity of clinical management and may have implications for the potential need to refine weight-management treatment to address pain.

CONCLUSIONS

A majority of Veterans with overweight/obesity in our sample also reported ≥1 painful condition. These patients also reported a very high burden of comorbidity, particularly those with ≥1 painful condition (i.e., the Veterans reporting ≥5 comorbidities were most likely to report 2 painful conditions). This multimorbidity may have a significant effect on the outcomes of existing weight-management programs, such as MOVE!, which may need to be modified to address pain management for optimal response among Veterans with these high-prevalence health concerns.

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Sex differences between Veterans participating in interdisciplinary chronic pain rehabilitation

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Abstract—The improved management of pain among the growing number of female Veterans receiving care through the Veterans Health Administration has been established as a priority, but studies suggest that females may respond differently to pain treatment. This study explored differences between female and male Veterans engaged in a Chronic Pain Rehabilitation Program and determined how female and male Veterans change following participation. Veterans (N = 324) in a 3 wk inpatient program completed self-report measures at admission, discharge, and 3 mo follow-up. Participants were 21% female (n = 67) and 79% male (n = 257). Compared with males, females were younger and less likely to be white or married/partnered. Females reported shorter pain duration and were more likely to have primary head or limb pain. At admission, fewer females were prescribed opioids than males and at lower doses. After opioid cessation in the program, however, there were no significant differences in use between the sexes at follow-up. Improvements in a range of domains were sustained at follow-up for both sexes, but females did not maintain gains in pain intensity or sleep while males reported more pain-related fear at discharge and follow-up. This study adds to the literature on sex-specific variations in chronic pain and implications for treatment.

Key words: chronic pain, females, gender, interdisciplinary treatment, multidisciplinary treatment, noncancer pain, opioids, pain rehabilitation, sex differences, treatment outcomes, Veterans, women.

INTRODUCTION

Chronic pain is prevalent among Veterans, and its treatment is a top priority for the Department of Veterans Affairs (VA) [1]. Female Veterans, whose use of VA healthcare has almost doubled in the last decade, are the fastest growing subset of the Veteran population [2]. It is projected that women will comprise 10 percent of the population treated in the VA by 2018 and over 14 percent by 2033 [3]. Female Veterans are younger on average than men, with 42 percent between the ages of 18 and 44, while only 13 percent of males are under 45 [2]. Among Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF), and Operation New Dawn (OND) Veterans, 51 percent of women are younger than 44 yr old [4]. In addition, female Veterans are more heterogeneous racially and ethnically, with 39 percent endorsing a minority background versus 23 percent of males [2].

Abbreviations: ANOVA = analysis of variance; CBT = cognitive behavioral therapy; CNP = chronic noncancer pain; CPRP = Chronic Pain Rehabilitation Program; CPS = chronic pain syndrome; CT = catastrophizing subscale; IMMPACT = Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials; MED = morphine equivalent dose; NRS = numeric rating scale; OEF = Operation Enduring Freedom; OIF = Operation Iraqi Freedom; OND = Operation New Dawn; POQ-VA = Pain Outcomes Questionnaire-VA; SIS = Symptom Implausibility Scale; SPQ = Sleep Problems Questionnaire; VA = Department of Veterans Affairs.

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Data indicate that 57 percent of OIF/OEF/OND females have enrolled in and are using VA services [4]. Women most likely to enroll in VA care have greater psychosocial stressors such as low income, poor health status, and lack of social support [5].

Among the general population, chronic pain is more common in women than men [6]. Studies of experimental pain suggest that women exhibit heightened pain sensitivity [7], experience more intense and frequent pain [8], and report a broader range of pain locations [9]. There is less known about sex differences among the Veteran population specifically. In a large-scale study of OIF/OEF Veterans, the probability of having persistent pain did not differ between sexes, but women were more likely to experience moderate to severe pain [10]. Another study revealed that at years 1 through 7 postdeployment, women were more likely than men to have back, joint, and musculoskeletal pain, and the odds of having these conditions increased for women compared with men each year following deployment [11]. The most prevalent medical condition reflected in VA records for both sexes was musculoskeletal conditions at 55.9 percent for females and 48.5 percent for males [2].

The investigation of sex differences in nonpharmacological pain treatments is lacking and the data available are inconsistent. Jensen et al. found that women, but not men, undergoing cognitive behavioral therapy (CBT) with or without physical therapy exhibited improved health-related quality of life [12]. A study by Hansen et al. investigating various forms of back exercises found that men received greater benefit from conventional physiotherapy than women [13]. Krogstad et al. found that women had significantly more pain reduction than men 2 yr following conservative multimodal care for orofacial pain [14].

While the effectiveness of interdisciplinary pain rehabilitation is well established in the literature [15–17], there is a dearth of data comparing men and women in these settings. In a study of pain tolerance and pain program treatment outcomes between sexes, Edwards et al. found that females demonstrated greater improvement in pain-related disability while males showed more reduction in pain [18]. In addition, females with higher pain tolerances versus those with lower pain tolerances had greater improvements in pain, reduced pain-related interference with functioning, and more activity increases, while pain tolerance was not associated with positive treatment outcomes among males. A study of patients with fibromyalgia following an intensive, outpatient, interdisciplinary pain program showed a better outcome on some scales of the 36-Item Short Form Health Survey for males compared with females in a study by Hooten et al. [19]. Most similar to the current study, Keogh et al. compared 98 patients with complex pain syndromes who participated in a 3 to 4 wk group-based interdisciplinary pain management program at discharge and 3 mo follow-up [20]. Although both sexes showed similar gains at program completion, males maintained gains after 3 mo and females did not. Pieh et al. did not examine follow-up data but found that in a 5 wk daily outpatient pain program, females improved more than males despite there being no significant differences at program admission, including in areas such as pain duration, pain-related disability, and psychiatric comorbidities [21].

The growing number of female Veterans, many of whom will inevitably experience chronic pain, makes the acquisition of knowledge about their characteristics, conditions, and treatment of paramount importance to more effectively serve this population. While pain is a significant problem for both sexes in the VA, female Veterans may have additional risk factors for the development of chronic pain, such as higher rates of injury during initial training [22] as well as higher rates of depression [23] and military sexual trauma [24]. These factors and others may affect the optimal approach to pain care among females and the development of sex-specific pain programs.

To our knowledge, no previous studies have investigated sex differences in population characteristics or treatment outcomes within an interdisciplinary pain setting in the Veteran population. To address this issue, we compared multidomain treatment outcomes of female and male Veterans with chronic noncancer pain (CNP) who participated in a 3 wk residential interdisciplinary chronic pain treatment program. Participants were assessed at three time points: admission, discharge, and 3 mo follow-up. The first aim was to explore differences in demographic and clinical variables between the sexes. The second aim was to determine whether there were differences between how females and males changed over time in pain outcomes. The findings in the literature in this area are limited and mixed; however, based on the most similar study in a civilian population [20], we hypothesized that both groups would demonstrate improvements from admission to discharge but that males would maintain more gains than females at the 3 mo follow-up.

METHODS

Participants and Procedures

The current study is a retrospective data analysis of Veterans with CNP who were admitted to the inpatient Chronic Pain Rehabilitation Program (CPRP) at the James A. Haley Veterans' Hospital in Tampa, Florida, between August 2006 and April 2011. The CPRP is an intensive 3 wk residential, interdisciplinary chronic pain treatment program with a rehabilitation philosophy that seeks to assist those with CNP by teaching self-management skills that will improve quality of life and overall functioning. Patients who participate in the CPRP often have had little pain relief from various pharmacologic trials, interventional and surgical procedures, physical therapy, or complementary or alternative medicine approaches. They typically meet criteria for chronic pain syndrome (CPS) (International Classification of Diseases-9th Revision-Clinical Modification code 338.4) [25], which is defined as chronic pain with significant psychosocial dysfunction. CPS is characterized by unsuccessful pain relief through conventional medical treatments; functional impairment in most domains of life; and negative emotional factors related to pain such as depression, anxiety, and irritability. The CPRP uses a biopsychosocial approach and targets the physical and emotional effects of pain with a focus on active treatment modalities including graduated physical therapy, aquatic therapy, daily paced walking, relaxation techniques, occupational therapy, recreational therapy, individual psychotherapy, educational groups, and family interventions as appropriate.

In addition, effective medication management is an important program goal and includes cessation of all opioids and centrally acting muscle relaxants. The use of other nonopioid analgesics are reviewed at admission and adjusted throughout treatment. Each participant's medication records were reviewed for the period in which they participated in the CPRP to confirm opioid use status at admission and to extract a taper dose. For those on opioids at admission, initial daily opioid dosing was calculated from the medication records based on the highest opioid taper dose dispensed in the first 3 d of the program. This dose was converted to a morphine equivalent dose (MED) for comparison purposes using established methods [26].

A cognitive-behavioral, biopsychosocial model serves as the basis of treatment. Treatment in the CPRP provides 6 to 8 h per day of supervised therapeutic programming during 15 consecutive workdays, coupled with an additional 2 to 3 h of daily independent, goal-directed assignments (e.g., walking and exercise program, relaxation techniques). Weekend treatment includes recreational and social activities as well as twice-daily exercise, walking, and relaxation sessions.

Prior to CPRP admission, those interested in participating in the program were evaluated for medical and psychiatric stability. Medical needs that may have precluded patients from full engagement and maximum benefit, thus excluding them from participation, included further evaluation by cardiology, neurosurgery, or pulmonology. Psychological barriers for participation included psychiatric hospitalization or illicit drug use within 90 d prior to screening. Those excluded from admission but interested in participating in the program were provided with treatment recommendations and rescreened at a future date.

Measures

Outcome measures reported in this study were administered at three time points. All participants initially completed measures within the first 2 d of admission to the CPRP. Participants were readministered and completed measures within 2 d of discharge from the program. Finally, they were mailed the questionnaires with return postage at 3 mo postdischarge and returned the packet via standard U.S. Postal Service. Questionnaires measured pain intensity and treatment outcomes across the major pain-related domains of functioning, catastrophizing, and sleep. Data regarding medications were retrospectively extracted from participants' electronic medical records.

Pain intensity was assessed using an 11-point pain numeric rating scale (NRS) to measure "usual" (average) pain over the last week. NRSs are reliable and valid methods for assessing pain intensity [27]. The NRS was anchored with the phrases "no pain" (0) and "worst pain imaginable" (10). The "usual pain" scale has been found to be one of the best measures of pain intensity when compared with alternatives such as "current pain" or "worst pain" [28].

Pain treatment outcomes were assessed using the Pain Outcomes Questionnaire-VA (POQ-VA) [29], which is a multidomain pain assessment instrument developed and validated specifically for Veterans. The POQ-VA assesses treatment outcomes across the major pain-related domains of functioning identified by the Rehabilitation

Accreditation Commission (2002) as essential for comprehensive outcome measurement [29]. POQ-VA scales include interference with mobility, negative affect, vitality (i.e., strength and endurance), and pain-related fear (i.e., avoidance motivated by fear of pain or reinjury). The POQ-VA scales have been shown to have high internal reliability and good stability [30], strong generalizability, and good discriminant and concurrent validity, and they have demonstrated sensitivity to treatment-related change [31]. The POQ-VA also contains an experimental scale that was developed as a measure of highly improbable pain-related symptoms (the Symptom Implausibility Scale [SIS]). The SIS consists of 10 items describing a range of unusual pain symptoms or complaints.

Pain catastrophizing was assessed using the 6-item catastrophizing subscale (CT) from the revised 26-item Coping Strategies Questionnaire [32]. The CT has adequate internal consistency (0.72) and has been shown to negatively correlate with measures of activity [32]. Catastrophizing also has been positively correlated with depressive symptomatology [33–34], negative affectivity [35], exaggerated emotional response to aversive stimuli [36], and expectation of pain and psychological distress [37].

Sleep was assessed using the Sleep Problems Questionnaire (SPQ) [38]. The SPQ is a 4-item measure of the most typical symptoms of poor sleep in both healthy and distressed populations. Responses are based on the number of days during the week that each sleep symptom occurs, and these 0 to 7 item scores are summed for an overall sleep symptom measure. The scale has good internal consistency and validity [38].

Data Analysis

In preliminary analyses, the demographic and clinical characteristics of participants based on sex were compared using *t*-tests for continuous variables and chi-square tests for categorical variables. When categorical variables included more than two categories and the overall chi-square test was significant, subsequent Bonferroni-corrected group comparisons were conducted for each category. To determine whether demographic and clinical variables for which there were significant differences between groups should be considered as potential control variables, the interaction with each of these variables with sex was evaluated for the pain variables at admission. Those variables that had significant interactions with sex would be retained as control variables.

To examine longitudinal changes in pain outcome variables across the three time points, repeated-measures analyses of variance (ANOVAs) were conducted using SPSS version 19 (IBM Corporation; Armonk, New York). Initial analysis consisted of a 2 (group: females, males) × 3 (time: admission, discharge, follow-up) ANOVA for each outcome variable. The main effects of sex and time and interaction effects for sex × time were evaluated. Quadratic terms were included to determine whether there were nonlinear effects (e.g., plateaus or decrements in pain outcomes following improvement). Differences between males and females at each time point were evaluated using independent samples *t*-tests and within-group differences from admission to discharge and discharge to follow-up were evaluated using paired-samples *t*-tests. A *p*-value of 0.05 (two-tailed) was used for statistical significance. Effect sizes were calculated using Cohen's *d*. An effect size of 0.2 to 0.3 is considered small, 0.5 medium, and ≥0.8 large [39]. The study was powered at 0.80 to detect an effect size of $f = 0.25$ for the interaction between sex and time, assuming a per group sample size of 80 and alpha = 0.05. The study was also powered at 0.80 to detect an effect size of $f = 0.14$ for within-group change across the three measurement points.

RESULTS

Preliminary Analyses

Veterans ($N = 324$) completed self-report measures at admission, discharge, and 3 mo follow-up. Participants were 21 percent female ($n = 67$) and 79 percent male ($n = 257$). **Table 1** presents demographic and clinical characteristics of participants. Regarding demographic factors, there were several significant differences. Females were younger, with an average age of 47.19 yr, while males were 52.77 yr on average ($t(322) = 3.81$, $p < 0.001$). The majority of female participants in this study were unmarried and not cohabiting with a partner (67%, $n = 45$), compared with males who tended to be married or living with a partner (63%, $n = 162$) (χ^2 (1, $N = 324$) = 19.21, $p < 0.001$). Finally, females were less likely to be white (χ^2 (2, $N = 324$) = 6.86, $p = 0.03$), at 61 percent ($n = 41$) versus 76 percent ($n = 195$) of males. Regarding clinical factors, females had a shorter pain duration ($t(320) = 2.53$, $p = 0.01$) of 9.35 yr on average versus males at 12.99 yr on average. They were less likely to have a

Table 1.
Differences between sexes on demographic and clinical factors. Data presented as mean ± standard deviation or percentage.

Variable	Female (n = 67)	Male (n = 257)	p-Value
Age (yr)	47.19 ± 9.33	52.77 ± 11.01	<0.001
Education (yr)	14.25 ± 1.89	13.75 ± 2.60	0.14
Pain Duration (yr)	9.35 ± 7.95	12.99 ± 11.07	0.01
Taking Opioids at Admission	24	38	0.03
MED at Admission*	39.63 ± 24.68	69.31 ± 69.18	0.002
Taking Opioids at Discharge	18	17	0.83
Race			0.03
Black	28	19	
White	61[a]	76[b]	
Asian, American Indian, or Other	11	5	
Employment at Admission			0.23
Employed	10	16	
Unemployed	90	84	
Relationship Status			<0.001
Married or Living with Partner	33	63	
Not Married or Not Living with Partner	67	37	
Primary Pain Site			0.02
Back	45[a]	58[b]	
Limb	21[a]	10[b]	
Neck	9	12	
Head	12[a]	5[b]	
Other	13	15	

Note: Superscript letters refer to Bonferroni-corrected group comparisons that revealed significant differences between groups in this category at $p < 0.05$.
*Among those taking opioids.
MED = morphine equivalent dose.

primary complaint of back pain (females: 45%, n = 30; males: 58%, n = 149), but more likely to report primary pain location in head (e.g., headaches) (females: 12%, n = 8; males: 5%, n = 13) (χ^2 (4, N = 324) = 11.67, p = 0.02) or the limb (e.g., leg, arm) (females: 21%, n = 14; males: 10%, n = 26).

Regarding opioid use at admission, 35 percent of all participants were prescribed opioids; however, females were less likely to be prescribed opioids (24%) than males (38%) (χ^2 (1, N = 324) = 4.73, p = 0.03). Among participants who were taking opioids, females had lower MEDs at admission compared with males (t(62) = 3.18, p = 0.002). Per CPRP standard of care, no participants were taking opioids at discharge. At follow-up, 17 percent of all participants reported opioid use; however, there were no differences in opioid use between females (18%) and males (17%) (χ^2 (1, N = 312) = 0.05, p = 0.83).

Given the difference between sexes in the previously mentioned demographic and clinical factors, we evaluated whether any should be included as covariates by evaluating the effect of their interaction with sex on each outcome variable. Despite these differences, there were no significant interactions for sex × age, sex × marital status, sex × race, sex × pain duration, sex × primary pain location, or sex × opioid use for any outcome ($p > 0.05$); therefore, these variables were not included as covariates.

To evaluate differences between groups on pain outcomes at admission, we used t-tests. There were significant differences between groups on vitality, a scale measuring strength and endurance. Specifically, compared with males, females reported more pain-related interference in vitality (t(322) = –2.10, p = 0.04) (**Table 2**).

Change Over Time in Pain Outcomes by Sex

For pain intensity, there was a significant linear effect of time (F(1,321) = 16.70, $p < 0.001$). However, there was no group × time interaction (F(1,321) = 0.12, p = 0.73), quadratic group × time interaction (F(1,321) = 1.39, p = 0.24), or main effect for group (F(1,321) = 0.02, p = 0.88). There were no significant differences between sexes at any time point. Comparing time effects for each group separately indicated that both females and males

Table 2.
Mean ± standard deviation of outcome variables by group.

Variable	Admission	Discharge	Follow-Up
Average Pain Level			
Female	6.94 ± 1.57	6.07 ± 1.93	6.42 ± 2.48
Male	6.88 ± 1.73	6.19 ± 1.80	6.26 ± 2.06
Highest Pain Level			
Female	8.46 ± 1.43	7.97 ± 1.80	7.66 ± 2.28
Male	8.50 ± 1.29	7.95 ± 1.64	7.89 ± 1.85
Pain Interference in Mobility			
Female	25.00 ± 9.96	20.55 ± 10.70	21.34 ± 12.41
Male	25.06 ± 10.15	21.72 ± 10.55	22.97 ± 10.99
Pain-Related Negative Effect			
Female	27.88 ± 11.33	21.84 ± 11.98	25.70 ± 11.55
Male	28.05 ± 11.34	23.70 ± 11.95	27.55 ± 12.56
Pain Interference in Vitality			
Female	21.42 ± 4.43	16.39 ± 5.15	18.89 ± 5.27
Male	19.95 ± 5.27	15.92 ± 5.38	18.59 ± 5.24
Pain-Related Fear			
Female	10.88 ± 5.26	7.25 ± 4.27	8.64 ± 4.44
Male	11.77 ± 4.55	8.88 ± 4.75	10.60 ± 4.78
Implausible Symptoms			
Female	48.36 ± 18.46	32.04 ± 20.02	39.09 ± 24.39
Male	47.19 ± 20.75	35.96 ± 21.07	42.24 ± 24.11
Sleep			
Female	21.48 ± 5.76	15.73 ± 7.84	20.05 ± 8.65
Male	21.18 ± 6.86	17.80 ± 7.99	20.10 ± 7.79
Pain Catastrophizing			
Female	19.93 ± 8.89	12.33 ± 8.37	13.91 ± 9.24
Male	19.03 ± 9.56	13.00 ± 9.36	16.22 ± 10.31

reported improved pain from admission to discharge ($p < 0.05$). However, this reduction was only maintained at follow-up for males. That is, males reported improved pain from admission to follow-up ($t(255) = 5.19$, $p < 0.001$), whereas there was only a trend toward improvement in pain intensity for females from admission to follow-up ($t(66) = 1.74$, $p = 0.09$). Effect sizes calculated from admission to discharge indicate small effects for males ($d = 0.4$) and medium effects for females ($d = 0.5$), and small effects for both at follow-up ($d = 0.3$).

For pain-related fear, a significant linear effect of time was found ($F(1,318) = 26.17$, $p < 0.001$). There was also a significant main effect for group ($F(1,318) = 8.25$, $p = 0.004$) (**Figure**). Planned comparisons indicated that both groups demonstrated improvements from admission to discharge and from admission to follow-up ($p < 0.05$). However, comparing the sexes at each time point indicates that females and males reported equivalent levels of pain-related fear at admission ($t(322) = 1.37$, $p = 0.17$), but males reported higher levels of pain-related fear than females at discharge ($t(322) = 2.55$, $p = 0.01$) and follow-up ($t(318) = 3.03$, $p = 0.003$). Effect sizes calculated from admission to discharge indicated medium effects for

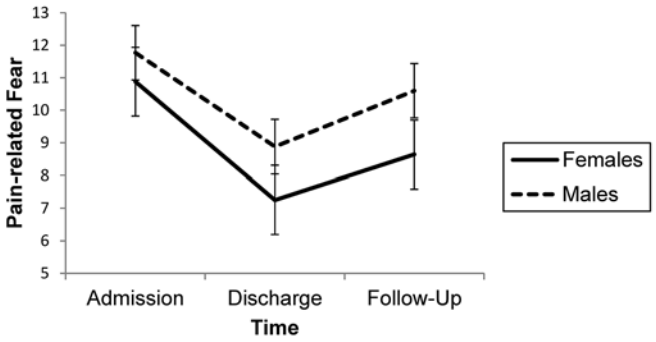

Figure.
Effect of sex on pain-related fear.

males ($d = 0.6$) and large effects for females ($d = 0.8$), which decreased at follow-up to small effects for males ($d = 0.3$) and medium effects for females ($d = 0.5$).

For mobility, a significant linear effect of time was found ($F(1,296) = 17.08$, $p < 0.001$). However, there was no group × time interaction ($F(1,296) = 0.87$, $p = 0.35$), quadratic group × time interaction ($F(1,296) = 0.01$, $p = 0.94$), or main effect for group ($F(1,296) = 0.47$, $p = 0.49$). There were no significant differences between sexes at any time point. Both females and males reported less pain-related interference with mobility from admission to discharge ($p < 0.05$), and both groups maintained this improvement at follow-up ($p < 0.05$), suggesting sex did not play a significant role in improvements in pain-related interference in mobility.

For pain-related negative affect, a significant quadratic effect of time was found ($F(1,317) = 64.46$, $p < 0.001$); however, the linear time effect was not significant ($p = 0.08$). There was no group × time interaction ($F(1,317) = 1.14$, $p = 0.29$), quadratic group × time interaction ($F(1,317) = 0.73$, $p = 0.40$), or main effect for group ($F(1,317) = 0.86$, $p = 0.36$). There were no significant differences between sexes at any time point. Both females and males reported improved pain-related negative affect from admission to discharge ($p < 0.05$), but these effects were not maintained at follow-up. That is, males returned to their pretreatment levels of pain-related negative affect by follow-up ($t(252) = 0.74$, $p = 0.46$) and females had only a trend toward improved affect from admission to follow-up ($t(66) = 1.71$, $p = 0.09$).

For vitality, a significant linear effect of time was found ($F(1,313) = 21.72$, $p < 0.001$). There was no group × time interaction ($F(1,313) = 1.18$, $p = 0.28$), quadratic group × time interaction ($F(1,313) = 0.03$, $p = 0.87$), or main effect for group ($F(1,313) = 1.50$, $p = 0.22$). At admission, females reported higher levels of pain-related interference in vitality; however, there were no significant differences between the sexes at discharge or follow-up. Both groups demonstrated improvements from admission to discharge and from admission to follow-up ($p < 0.05$), suggesting sex did not play a significant role in improvements in pain-related interference in vitality.

For implausible symptoms, a significant linear effect of time was found ($F(1,280) = 19.22$, $p < 0.001$). There was no group × time interaction ($F(1,280) = 1.60$, $p = 0.21$), quadratic group × time interaction ($F(1,280) = 0.00$, $p = 0.97$), or main effect for group ($F(1,280) = 0.22$, $p = 0.64$). There were no significant differences between sexes at any time point. Both groups demonstrated improvements from admission to discharge and from admission to follow-up ($p < 0.05$), suggesting sex did not play a significant role in improved reports of implausible symptoms.

For sleep, a significant linear effect of time was found ($F(1,303) = 5.13$, $p = 0.02$). There was no group × time interaction ($F(1,303) = 0.12$, $p = 0.73$), quadratic group × time interaction ($F(1,303) = 1.72$, $p = 0.19$), or main effect for group ($F(1,303) = 0.33$, $p = 0.57$). There were no significant differences between sexes at any time point. Comparing time effects for each group separately indicated that both groups demonstrated improvements from admission to discharge ($p < 0.05$). However, at follow-up this reduction was only maintained for males. That is, males reported improved overall sleep from admission to follow-up ($t(244) = 2.21$, $p = 0.03$), whereas the change for females from admission to follow-up was not significant ($t(60) = 1.38$, $p = 0.17$). Effect sizes calculated from admission to discharge indicated medium effects for males ($d = 0.5$) and large effects for females ($d = 0.8$), which decreased for both groups at follow-up to small effects ($d = 0.1$ and 0.2, respectively).

For catastrophizing, a significant linear effect of time was found ($F(1,304) = 23.41$, $p < 0.001$). There was no group × time interaction ($F(1,304) = 2.45$, $p = 0.12$), quadratic group × time interaction ($F(1,304) = 0.00$, $p = 0.99$), or main effect for group ($F(1,304) = 0.75$, $p = 0.39$). There were no significant differences between the sexes at any time point. Both groups demonstrated improvements from admission to discharge and from admission to follow-up ($p < 0.05$), suggesting sex did not play a significant role in improvements in pain catastrophizing.

DISCUSSION

Consistent with previous findings, this study provides additional support regarding the benefits of interdisciplinary pain rehabilitation across a range of domains for both males and females. The results of this retrospective examination supported our hypothesis that while both males and females demonstrated significant improvements from admission to discharge, males maintained more gains than females at follow-up. The differential effects between sexes suggest potential considerations for future clinical care and investigation to maximize the benefits of interdisciplinary chronic pain treatment.

Distinctions were found among sexes in several areas. Demographically, females were younger, less likely to be white, and less likely to be married or partnered. They had shorter pain durations, were less likely to have back pain, more likely to have head or limb pain, and less likely to be prescribed opioids. If taking opioids, they were on a lower daily MED. At admission, females reported more pain-related interference in vitality (i.e., strength and endurance), but there were no differences at discharge or follow-up. At discharge, both males and females reported significant improvements on all outcome variables; however, there were differences between males and females at the 3 mo follow-up.

While both sexes reported improved pain intensity from admission to discharge, females did not maintain pain reduction gains at 3 mo follow-up. This is similar to Keogh et al.'s finding, where females returned to baseline levels of pain intensity versus males [20]. While both sexes had statistically significant decreases in pain intensity at discharge, the effect sizes for females were medium, indicating a clinically significant change [29], whereas the effect size for males was small, meaning females actually made greater gains while in the program but were unable to maintain them. At 3 mo, effect sizes were small across sexes; however, it is important to note that the treatment modality is a tertiary-level inpatient pain rehabilitation program in which the population served represents those individuals who have the most chronic and treatment-refractory conditions. Because of this, the focus is on improving quality of life and function across domains despite the chronicity of the pain condition and any decrease in pain intensity is noteworthy.

In addition, while overall sleep improved during the course of program participation for both sexes, only males maintained gains in overall sleep at follow-up. The gains for both at discharge were statistically significant and the effect size for females was large, indicating a clinically significant change [29], whereas the effect size for males was medium. As with pain, females made greater gains while in the program but were unable to maintain them, and effects across sexes were small at 3 mo. While greater clinical significance at follow-up would have been preferred, the prevalence of sleep issues in the treated population, including sleep-disordered breathing conditions and medical comorbidities, make even small changes meaningful.

On the variable related to avoidance of activity due to a fear of increased pain and/or reinjury, females and males were equivalent at admission and both sexes demonstrated significant improvement over time; however, males reported higher levels of pain-related fear than females at both discharge and follow-up. Interestingly, in a study of sex and gender in the experience of pain, Ramírez-Maestre and Esteve found that fear-avoidance was associated with pain intensity in males but not females [40].

Both groups maintained improvements in mobility, vitality, endorsement of implausible symptoms, and catastrophizing. While some previous studies have found that females reported higher levels of catastrophizing, the results of the present study are consistent with Ramírez-Maestre and Esteve [40] and Unruh et al. [41] who did not find sex differences in this variable. Both females and males reported improved negative affect at program discharge, but the effects were not maintained for either group at follow-up.

This study highlights several areas for future research and clinical consideration. While the efficacy of interdisciplinary pain care has been well established in the literature, there is limited research examining sex differences in this treatment modality and available studies reflect inconsistent outcomes. Increased attention is warranted, and focusing on why and how specific aspects of treatment may affect the sexes differently would be particularly beneficial to enhance understanding. This would help to shed light on treatment decisions and inform whether programs should be altered based on the specific needs of females. Furthermore, future research should evaluate whether an intervention targeted to females can produce stronger effects and what aftercare treatment is most effective at maintaining those effects.

Across the literature regarding female Veterans with pain, the population is younger, and less likely to be white or married than their male peers. These consistent demographic findings have several potential implications. Females in the VA are more likely to be transitioning from the military and concomitantly contemplating choices about pursuing employment or additional education. Since they are more ethnically and racially diverse, it is essential to be aware of how their preferences and needs may differ. The fact that they are less likely to be married highlights the importance for independence both financially and in the home, as well as the potential implications of single parenting. When considering the treatment of females with pain or developing sex-specific programs, focusing on areas such as adjustment and transitional issues,

vocational options, culturally sensitive diversity topics, gender roles (including parenting), and independent functioning should be emphasized. As is true of females in the general population, headaches were more common among females in this study. Because of this, it is also important to consider an enhanced role for the evaluation and treatment of headaches within pain rehabilitation programs.

Examining differences in VA and Department of Defense prescribing practices for females versus males also warrants further investigation. While lower dosing is likely, at least in part because of average weight differences between the sexes, in this study, females were also less likely to be prescribed opioids at all. This finding conflicts with evidence from the public sector that females are actually more likely to be prescribed opioids. The reasons for the opioid use patterns in this sample are unclear, although there are several possibilities. Since chronic opioid therapy is typically not indicated for headache pain, which was more prevalent among females, that may account for some of the difference. Females may have received higher dosages of other analgesics such as muscle relaxants, though we do not know because medications other than opioids were not assessed at admission. It is also possible that females were undertreated or undermedicated compared with males [42]. Additionally, the literature indicates that females are more likely to be referred to mental health specialists when presenting for pain complaints [41].

Perhaps the most important issue that this study raises is determining the optimal follow-up needs for females as well as males following intensive rehabilitation. Effect sizes ranged from small to large at discharge and tended to decrease at follow-up. This trend indicates that all patients would likely benefit from additional maintenance treatment following program discharge to sustain effects. Programmatically, clinical responses in the CPRP have been to schedule an earlier postdischarge visit or contact (i.e., at 1 mo vs 3 mo) to evaluate implementation and make any needed interventions as soon as possible. Aftercare options have also been expanded to include several stepped groups to expand duration. However, although effect sizes were generally small at follow-up, suggesting limited clinical significance, the modest improvements should be balanced against the fact that those in the program had longstanding CPS and the vast majority of Veterans who tapered off of opioid analgesics during treatment did not return to use.

While females did as well as or better than males during treatment, their self-reported pain intensity did not remain significantly improved 3 mo after discharge, which was consistent with previous findings [20]. They also did not retain sleep gains, and neither group maintained improvements in negative affect at follow-up. For females, since they made greater gains in several areas during treatment but did not maintain them, enhanced aftercare should be considered strongly in any sex-specific pain programs. Identifying specific information about why regression for both sexes may have occurred is important in understanding how to prevent the return to baseline functioning in these areas in the future. Clarification regarding the obstacles that may have prevented the implementation of acquired self-management strategies would be useful in the development of an enhanced plan of care prior to discharge and may improve long-term outcomes. Furthermore, since the cohort that receives comprehensive tertiary-level care is likely to have greater psychiatric needs than the general chronic pain population regardless of sex, more intensive mental health support following treatment may be indicated, as the lack of maintenance regarding affective gains suggests.

Finally, the consideration of issues more prevalent among female Veterans should be examined in future research and treatment approaches. For example, since military sexual trauma is reported at screening among one in four female Veterans [43], consideration of options that address both physical pain and trauma are indicated to optimize the efficiency and effectiveness of treatment. Likewise, tailoring treatment to accommodate conditions seen most commonly in females such as headaches, fibromyalgia, and pelvic pain may better serve the needs of this special population. Furthermore, some evidence suggests that using a different therapeutic approach with females such as Acceptance and Commitment Therapy may be more beneficial than a CBT-guided curriculum focused on controlling or changing unwanted thoughts and feelings.

The current study has several limitations that should be acknowledged. First, this was a retrospective design that did not include a control group; thus, no definitive conclusions can be made regarding the intervention. Second, only pain location and negative affect, as reflected on the POQ-VA, were known for program participants. Specific medical and psychiatric diagnostic information was not available and likely would have been helpful in gaining a fuller understanding of the role of comorbidities.

Third, the generalizability of this sample to the general population may be restricted because it was only 21 percent female and all participants had a military history. However, given that females constitute slightly less than 10 percent of the cohort registered for VA care, the higher number of females in this sample likely accurately reflects the prevalence of chronic pain among female Veterans. In addition, having only one point of follow-up at 3 mo was a limitation because we were unable to examine sustained differences over a longer period such as 6 or 12 mo. Finally, while this was not a clinical trial, the use of Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT)-recommended measures might have helped in making conclusions more standardized and generalizable. The selected measures were chosen for use in a clinical program due to their applicability to the population; specifically, the POQ-VA is the only pain outcomes measure that was developed and validated for Veterans. Furthermore, IMMPACT core domains such as pain intensity and various key functional areas such as negative affect and mobility are reflected in the POQ-VA.

CONCLUSIONS

The current findings add to a growing body of research suggesting that sex differences may exist in the determinants of pain treatment outcomes. Given the increase in the number of female Veterans entering the VA system, these data are likely to address gaps in our current knowledge of female Veterans' experiences and needs in pain management and have clinically relevant implications for better serving female Veterans with chronic pain. Additional examination of the differences that may exist between sexes and their implications for effective pain management should continue to be explored.

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Statistical analysis and interpretation of data: K. M. Phillips, S. Rafie.
Drafting of manuscript: J. L. Murphy, K. M. Phillips, S. Rafie.
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Potential neurobiological benefits of exercise in chronic pain and posttraumatic stress disorder: Pilot study

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Abstract—This pilot study assessed the effects of cardiopulmonary exercise testing and cardiorespiratory fitness on plasma neuropeptide Y (NPY), allopregnanolone and pregnanolone (ALLO), cortisol, and dehydroepiandrosterone (DHEA), and their association with pain sensitivity. Medication-free trauma-exposed participants were either healthy ($n = 7$) or experiencing comorbid chronic pain/posttraumatic stress disorder (PTSD) ($n = 5$). Peak oxygen consumption (VO_2) during exercise testing was used to characterize cardiorespiratory fitness. Peak VO_2 correlated with baseline and peak NPY levels ($r = 0.66$, $p < 0.05$ and $r = 0.69$, $p < 0.05$, respectively), as well as exercise-induced changes in ALLO ($r = 0.89$, $p < 0.001$) and peak ALLO levels ($r = 0.71$, $p < 0.01$). NPY levels at the peak of exercise correlated with pain threshold 30 min after exercise ($r = 0.65$, $p < 0.05$), while exercise-induced increases in ALLO correlated with pain tolerance 30 min after exercise ($r = 0.64$, $p < 0.05$). In contrast, exercise-induced changes in cortisol and DHEA levels were inversely correlated with pain tolerance after exercise ($r = –0.69$, $p < 0.05$ and $r = –0.58$, $p < 0.05$, respectively). These data suggest that cardiorespiratory fitness is associated with higher plasma NPY levels and increased ALLO responses to exercise, which in turn relate to pain sensitivity. Future work will examine whether progressive exercise training increases cardiorespiratory fitness in association with increases in NPY and ALLO and reductions in pain sensitivity in chronic pain patients with PTSD.

Abbreviations: ALLO = allopregnanolone and pregnanolone, ANOVA = analysis of variance, BMI = body mass index, CPT = cold pressor test, CPX = cardiopulmonary exercise testing, CSF = cerebrospinal fluid, CSU = clinical studies unit, CV = coefficient of variation, DHEA = dehydroepiandrosterone, DHEA(S) = DHEA-sulfate, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-4th Edition, EKG = electrocardiogram, GABA = gamma-aminobutyric acid, GC-MS = gas chromatography-mass spectrometry, IV = intravenous line, NPY = neuropeptide Y, OEF = Operation Enduring Freedom, OIF = Operation Iraqi Freedom, PTSD = posttraumatic stress disorder, RIA = radioimmunoassay, TC = trauma-exposed healthy control, VA = Department of Veterans Affairs, VO_2 = oxygen consumption.

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Key words: ALLO, biomarkers, cardiorespiratory fitness, chronic pain, exercise, neurosteroids, NPY, pain sensitivity, PTSD, VO_2.

INTRODUCTION

Chronic pain and posttraumatic stress disorder (PTSD) are both disabling and health-threatening conditions that adversely affect the biological, psychological, and social domains of those affected and place a significant financial strain on the healthcare system [1]. Although reported rates vary, as many as 50 to 75 percent of patients who present for PTSD treatment also have a significant chronic pain condition [2–4]. Conversely, among persons presenting for treatment of chronic pain, approximately 20 to 37 percent have PTSD [5]. Furthermore, 80 percent of combat Veterans with PTSD report experiencing chronic pain [6]. While the relationship between chronic pain and PTSD has been observed across all combat theaters, it may be particularly strong among Operation Iraqi Freedom (OIF)/Operation Enduring Freedom (OEF) Veterans because the pain and PTSD conditions in these Veterans are more likely to have a recent onset and to be associated with the same traumatic event [7]. The most recent estimates from a study by Cifu et al. of a nationally representative sample of OIF/OEF/Operation New Dawn Veterans receiving care at Department of Veterans Affairs (VA) polytrauma clinics estimated prevalence rates of chronic pain to be approximately 42 percent [8] (as compared with 11% in the general population) [9]. PTSD rates were 29.4 percent (vs 8% in the general population) [2], and the comorbid chronic pain and PTSD rate was 12.6 percent. Despite the differences in these estimates, the strong relationship between chronic pain and PTSD is clear and the coprevalence of these conditions negatively affects the course of both disorders [1–2].

Research suggests that the relationship between chronic pain and PTSD is maintained by biological as well as psychosocial factors such as comorbid depression, anxiety sensitivity, poor perceived life control, and physical disability [9]. However, while biopsychosocial models of the relationship between chronic pain and PTSD have focused on different empirically supported aspects of the chronic pain-PTSD relationship (e.g., mutual maintenance, shared vulnerability, triple vulnerability, and fear avoidance models) [1–2,10–12], descriptions of the biological contribution are often limited. For example, vulnerability to increased physiological arousal is raised as a relevant pathophysiological process without a clear description of specific neurobiological factors involved. We suggest that to be truly consistent with a biopsychosocial model of illness, the mechanisms underlying the biological contribution to these two disorders should be further examined and delineated. Such an investigation could enable development of novel and more effective pharmacological and nonpharmacological treatments targeted to biological mechanisms that promote comorbid chronic pain and PTSD—treatments that could potentially be individually tailored. This is particularly compelling at a time when the VA is focused on developing alternatives to opiate-based treatments to reduce the effect of comorbid chronic pain and PTSD on the lives of Veterans.

As detailed in a recent review [13], potential pathophysiologic factors shared between chronic pain and PTSD include deficits in neuropeptide Y (NPY) and the neuroactive gamma-aminobutyric acid (GABA)-ergic steroids allopregnanolone and its equipotent stereoisomer pregnanolone (together termed ALLO) [14–20]. These antinociceptive and stress-buffering molecules have been found to be low in patients with PTSD and inversely correlated with PTSD symptom severity [14–25]. Given the known antinociceptive properties of NPY and ALLO [15,17–18,20], these molecules also may be low in chronic pain populations exposed to trauma. Previous animal and human studies have shown that exposure to repeated, severe, or life-threatening stress is associated with reductions in resting plasma NPY levels, which are, in turn, associated with increased release of norepinephrine under stress [25]. It is not yet clear whether NPY responses to stress differ between trauma-exposed individuals with and without PTSD. Less is known about the role of trauma exposure versus PTSD vulnerability in relation to ALLO resting levels or stress reactivity. The study that demonstrated a strong correlation between low cerebrospinal fluid (CSF) levels of ALLO in women with PTSD and PTSD reexperiencing symptoms utilized a non–trauma-exposed comparison group [16].

In addition to these inhibitory central nervous system neurosteroids, it is important to consider other neuroactive steroids that are important to acute and long-term stress adaptation and that modulate the NPY and ALLO systems. For example, there is a glucocorticoid response element in the promoter of genes involved in both NPY and ALLO synthesis. Of note, cortisol is thought to be of benefit in acute pain conditions, although sustained high

levels of cortisol have been found to play a role in chronic pain [26]. The androgen dehydroepiandrosterone (DHEA) is secreted at the same time as cortisol and negatively modulates $GABA_A$ receptor function while positively modulating excitatory N-methyl-D-aspartate receptor function. Thus, DHEA may acutely antagonize effects of ALLO in neuronal systems, consistent with the observation that higher CSF DHEA/ALLO ratios were associated with increased PTSD reexperiencing and negative mood symptoms in premenopausal women. On the other hand, DHEA also enhances the metabolism of cortisol to an inactive metabolite, and administration of DHEA has been associated both with reductions in plasma cortisol levels and increases in plasma ALLO levels, as well as relief of negative mood. In addition, a higher plasma DHEA to cortisol ratio has been shown to correlate negatively with PTSD and negative mood symptoms [27]. Thus, by including cortisol and DHEA in our preliminary investigation, we hoped to compare profiles of these interacting neuroendocrine factors between chronic pain/PTSD and trauma-exposed healthy controls (TCs).

It is thus of interest that acute intense exercise induces NPY release in healthy humans [28–29] and that rodents show acute increases in plasma and brain allopregnanolone levels after acute swim stress [30–33]. Exercise is also known to increase vagal parasympathetic, as well as sympathetic, neurotransmission and thus has the potential to suppress proinflammatory pathways and thereby reduce pain [34]. We thus hypothesized that an acute exercise challenge test might serve as a method to acutely raise plasma NPY and ALLO levels and affect pain sensitivity, as well as delineate differences in NPY and ALLO physiology between a chronic pain/PTSD population and TCs. We hypothesized that (1) acute exercise-induced changes in NPY and ALLO would be positively correlated with cardiorespiratory fitness, as measured by peak oxygen consumption (VO_2) during exercise testing, as well as with pain threshold and tolerance after exercise testing, and that (2) baseline levels and reactivity of NPY and ALLO would be lower in the chronic pain/PTSD group than in TCs. Given the variety of interactions between cortisol, DHEA, ALLO, and NPY and the variability in findings for cortisol and DHEA across different pain and PTSD populations [27,35], we did not expect to see clear relationships between pain sensitivity and exercise-induced increases in cortisol or DHEA in this small pilot sample.

METHODS

Participants

Twelve participants with and without chronic pain and PTSD were included in this study of the effect of a single session of peak cardiopulmonary exercise testing (CPX) on plasma neurohormone levels (NPY, ALLO, cortisol, DHEA) and pain sensitivity. Seven participants comprised the TC group, and five participants comprised the chronic pain/PTSD group. Approximately 58.3 percent of the sample (n = 7) were male and 25 percent were Veterans (n = 3), all of whom were in the chronic pain/PTSD group. Participants were of several races: African American (42%), Caucasian (33%), Asian (8%), and other (Native American and Indian, 16.7%).

Diagnostic evaluations were conducted by licensed healthcare professionals. The Clinician-Administered PTSD Scale, based on the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV) [36], was used to diagnose and score severity of PTSD. The Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition [37] was administered to evaluate comorbid psychological disorders. A physical examination, routine laboratory testing, urine testing for illicit substances and cotinine (a by-product of nicotine), and an electrocardiogram (EKG) were administered to establish general health, confirm freedom from substance abuse, and establish safety for participation in the CPX. Chronic pain was established initially through participant self-report of musculoskeletal pain for a minimum of 3 mo with an overall pain intensity of 4 or greater on a 0–10 numerical pain rating scale. These participants were then evaluated by a rehabilitative medicine doctor and given an appropriate International Classification of Diseases-9th Revision diagnosis for musculoskeletal pain, as well as medical clearance from a pain perspective for participation in exercise testing. All study participants were free of psychotropic medications for at least 6 wk and free of pain medications for five half-lives (~24 h in most cases) prior to testing.

Experimental Procedures

See the **Appendix** (available online only) for a flowchart of study procedures. Once eligibility was confirmed, participants presented for the exercise testing session at a clinical studies unit (CSU). The entire session took place between 8 a.m. and about 12 p.m. In addition to our stringent inclusion/exclusion criteria, participants were

instructed to abstain from food and beverages, except for water, after midnight before testing. Upon arrival at the CSU, the subjects were given water and power bars (6 kcal/kg) to provide the same relative caloric load across participants. An intravenous line (IV) was placed and the "breakfast" provided 2 hr before pre-exercise baseline blood sampling to ensure that stress and feeding-induced increases in adrenocorticotropic hormone, cortisol, glucose, and other reactants such as ALLO [32] had returned to baseline. During this time, participants completed non-provocative self-report questionnaires about mood, pain interference, exercise motivation, and overall distress (results not reported in this article).

After baseline blood sampling, a cold pressor test (CPT) [38] was conducted to assess pain sensitivity prior to exercise. The CPT was repeated 30 min after CPX was completed. The CPT has been used widely in laboratory studies to measure pain perception and tolerance [39], as well as in investigations of the role of hypothalamic-pituitary-adrenal axis activation in pain [40]. During the CPT, participants were instructed to hold their right hand still up to the wrist in temperature-controlled water (4°C) inside the cold pressor apparatus. They were instructed to say when they first experienced pain and to withdraw the hand when the pain became intolerable. Two measures of pain sensitivity were derived: "pain threshold" and "pain tolerance." Pain threshold is defined as the number of seconds between hand immersion in the ice water and the first report of "pain" and is considered to correspond to physiological aspects of pain perception [39]. Pain tolerance is defined as the number of seconds between hand immersion and withdrawal from the water and is considered to correspond to the psychological aspects of pain perception. Finally, unknown to the participant, a maximum time limit of 7 min was imposed for safety purposes. A second blood draw was performed 15 min after the CPT, about 5 min before CPX.

CPX was performed in accordance with guidelines published by the American College of Cardiology [41]. Once ready for CPX, the participant was transported to the exercise testing room via wheelchair and transferred to the recumbent cycle ergometer. EKG electrodes were applied. The CPX was completed using a progressive staged cycle protocol, during which a ventilatory expired gas analysis system (MedGraphics BreezeSuite; St. Paul, Minnesota) was used to measure continuous gas exchange. Telemetry, blood pressure, and oxygen saturation were assessed for each subject 1 min prior to, during, and following the exercise test in standard clinical fashion. Peak VO_2 was defined as the 30 s averaged value during the last stage of the CPX for use as the primary gauge of cardiorespiratory fitness. Ventilatory anaerobic threshold was also assessed as a measure of submaximal performance, determined as a 10 s average by the V-slope method [42]. All subjects achieved a peak respiratory exchange ratio of ≥1.05, a standard indicator of adequate exercise effort. Blood was again collected via IV 5 min and 30 min after completion of exercise.

Neurohormone Assays

On the day of the CPX, collected blood was placed immediately on wet ice and spun within 15 min of collection in a refrigerated centrifuge for 15 min. Plasma was then aliquotted into Eppendorf tubes for storage at –80°C until assays were performed. Plasma concentrations of NPY were measured without extraction using a direct radioimmunoassay (RIA) kit (Euro-Diagnostica-ALPCO Diagnostics; Salem, New Hampshire). The assay sensitivity is ~12.81 pg/mL and has <0.1 percent crossreactivity with $NPY_{22–36}$, peptide YY, pancreatic polypeptide, and other neuropeptides. The intra-assay coefficient of variation (CV) is 4.7 percent, and the interassay CV is 8.4 percent. Plasma levels of ALLO were measured by gas chromatography-mass spectrometry (GC-MS) after separation of the steroids by high-performance liquid chromatography using previously published methods [43–44]. ALLO levels were identified based on their GC-MS retention time characteristics; the definitive structural identification of each neurosteroid is provided by its unique mass fragmentation pattern. Only peaks with a signal-to-noise ratio greater or equal to 5:1 were integrated. The limit of neurosteroid detection with this method is 1 pg (femtomolar sensitivity). Intra-assay CVs range between 2 and 7 percent for each neurosteroid. Concentrations of cortisol were measured by a solid-phase RIA (Siemens Healthcare Diagnostics; Deerfield, Illinois) with an intra-assay CV of approximately 4 percent and interassay CV of approximately 6 percent. The standard range is from 0.5 to 50 μg/dL, with an assay sensitivity of 0.3 μg/dL. Plasma concentrations of DHEA were measured by an RIA that requires no prior sample extraction (Beckman Coulter; Chino, California). The antiserum crossreacts 100 percent with DHEA but demonstrates low crossreactivity to other steroids potentially present in subject samples (e.g., crossreactivity to DHEA-sulfate [DHEA(S)] is 0.02%). The intra-assay CV is approximately 4 percent, while the interassay CV

is approximately 7 percent. The standard working range is 0.2 to 24 ng/mL, with a theoretical sensitivity of 0.06 ng/mL.

Data Analytic Plan

The distributions of variables under investigation were tested for normality using the Kolmogorov-Smirnov test, and nonparametric statistical approaches were then employed as appropriate. Thus, to address hypothesis 1, Spearman rather than Pearson correlations were used. Plasma DHEA(S) levels were normalized by age because DHEA(S) levels are known to normally decline significantly over the age range of the study participants [45]. Levels of plasma NPY, ALLO, cortisol, and DHEA(S) were also normalized by body mass index (BMI) when correlated with peak VO_2, which is expressed in milliliters per kilogram per minute. For initial correlations with pain sensitivity, absolute neuroactive hormone levels were used, given that the effect of these neuromodulators within local pain circuits or the brain would not be expected to vary by weight. However, given the absence of standards in the field for such analyses, we repeated these analyses using hormone levels normalized by weight. To address hypothesis 2 and test for the presence of group differences in hormone levels and responses to the CPX, repeated-measures analyses of variance (ANOVAs) were conducted with and without inclusion of BMI as a covariate. Finally, given the small size of this pilot sample, partial eta squared values were reported with each *F*-value in order to better estimate the strength of each finding. Such values were interpreted based on guidelines by Cohen [46]: 0.01 = small; 0.06 = medium; 0.13 = large.

RESULTS

The mean age of the sample was 39.0 ± 10.3 yr. In the pain/PTSD group, two participants had current comorbid major depression, one was diagnosed with simple phobia, one was diagnosed with generalized anxiety disorder, one was diagnosed with lifetime alcohol dependence, one was diagnosed with lifetime substance dependence, and two were diagnosed with a lifetime eating disorder. In the TC group, two participants met criteria for lifetime depression (episode) and one for lifetime alcohol abuse. No participants met criteria for a psychotic disorder. All were free of prescribed and illicit drugs, as well as alcohol, for a minimum of 4 wk before participating in exercise testing, and all were free from significant medical illnesses. BMI was calculated using height and weight taken on the day of the exercise test session. For both groups combined, BMI ranged from 18.9 (normal weight) to 51.9 (obese class III), with a mean BMI of 34.9 ± 9.92 (obese class I). The two groups significantly differed in BMI: Mean $(M)_{TC}$ = 30.3 ± 9.4 (Obese class I), $M_{pain/PTSD}$ = 41.5 ± 6.8 (obese class III); $t(10) = -2.41$, $p < 0.05$. For both groups combined, VO_2 ranged from 5.9 (very poor fitness) to 46.5 (excellent fitness), with a mean VO_2 of 22.1 (poor fitness). The two groups did not significantly differ in VO_2: M_{TC} = 24.8 ± 13.2, $M_{pain/PTSD}$ = 18.3 ± 4.8; $t(10) = 1.04$, $p = 0.32$.

Neuropeptide Y

Figure 1(a) shows individual NPY levels for all participants across the four time points.

A repeated-measures ANOVA with Greenhouse-Geisser corrections showed that NPY levels did not change significantly across time in this small sample ($F(1.31,11.74) = 2.97$, $p = 0.10$; partial $\eta^2 = 0.25$), although there was a large effect size. There was not a significant difference in NPY levels between groups ($F(1,9) = 0.33$, $p = 0.58$; partial $\eta^2 = 0.04$), nor was the time by group interaction significant ($F(1.31,11.74) = 0.15$, $p = 0.77$, partial $\eta^2 = 0.02$). When the analysis was repeated using BMI as a covariate, the effect sizes were similar. For all study participants, there was a positive correlation between VO_2 peak and NPY levels measured at baseline ($r = 0.66$, $p < 0.05$) and peak exercise ($r = 0.69$, $p < 0.05$). NPY levels at peak exercise were positively correlated with pain threshold measured 30 min after exercise ($r = 0.65$, $p < 0.05$). NPY levels normalized by BMI did not correlate significantly with indices of pain sensitivity (i.e., pain threshold or tolerance).

Allopregnanolone and Pregnanolone

Figure 1(b) shows individual ALLO levels for all participants across the four time points. A repeated-measures ANOVA with sphericity assumed revealed significant differences in ALLO levels across time ($F(3,27) = 18.01$, $p < 0.001$, partial $\eta^2 = 0.67$); post hoc analyses revealed significant increments in ALLO between successive time points ($p < 0.006$ to 0.001). There was not a significant difference in ALLO levels between groups ($F(1,9) = 0.83$, $p = 0.39$, partial $\eta^2 = 0.08$) or a significant group by time interaction ($F(3,27) = 0.98$, $p = 0.39$, partial $\eta^2 = 0.10$). These latter findings represented medium to large effect sizes, however, suggesting that the lack of

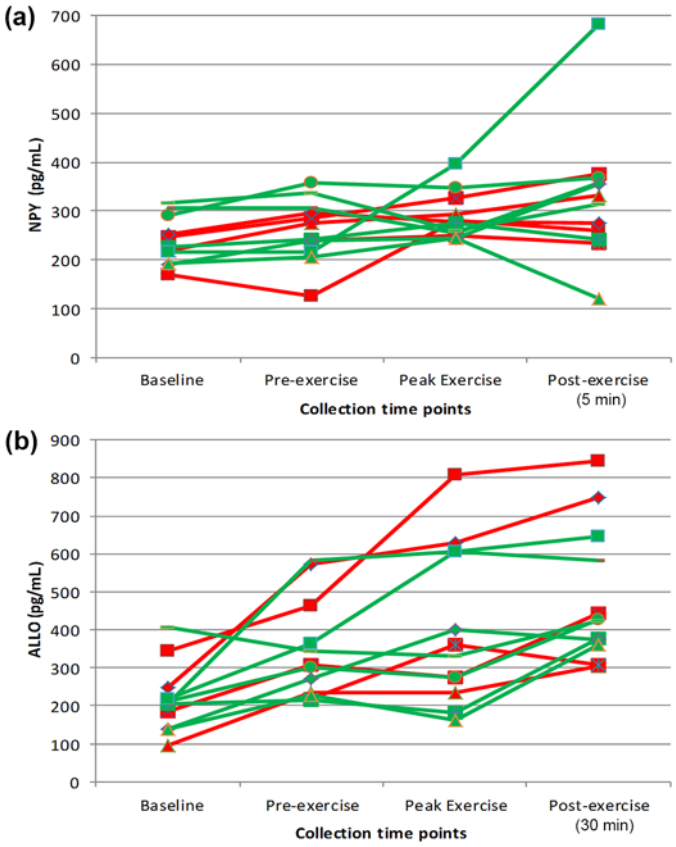

Figure 1.
(a) Plasma neuropeptide Y (NPY) levels for individual participants across four study time points at which it was measured: baseline, pre-exercise, peak of exercise, and 5 min after exercise. **(b)** Plasma allopregnanolone and pregnanolone (ALLO) levels for individual participants across four time points at which it was measured: baseline, pre-exercise, peak of exercise, and 30 min after exercise. Red = posttraumatic stress disorder/chronic pain participants, Green = trauma-exposed healthy participants. Note that pre-exercise cold pressor test was administered between baseline and pre-exercise time points.

statistical significance was due to the small sample size. When these analyses were repeated using BMI as a covariate, there were similar findings across time points: a large effect size for the group by time interaction and a significant group difference ($F(1,8) = 7.12$, $p < 0.05$), such that PTSD participants had higher ALLO levels over time than the TC group.

For all study participants, there was a positive correlation between peak VO_2 and peak ALLO measured 30 min after exercise ($r = 0.71$, $p < 0.01$). There were also positive correlations between VO_2 and the increase in ALLO from the baseline and pre-exercise time points to 30 min after exercise ($r = 0.64$, $p < 0.05$ and $r = 0.89$, $p < 0.001$, respectively). The increase in ALLO from pre-exercise to 30 min after exercise was positively correlated with pain tolerance after exercise ($r = 0.64$, $p < 0.05$). When ALLO was normalized by BMI, there were no significant correlations with indices of pain sensitivity.

Additional Neuroendocrine Factors

Cortisol

Figure 2(a) shows mean cortisol levels by group across the three time points at which it was measured. A repeated-measures ANOVA, using BMI as a covariate and with sphericity assumed, showed no significant change in cortisol levels across time points ($F(2,18) = 1.08$, $p = 0.36$, partial $\eta^2 = 0.11$), although there was a large effect size. Nor was there a significant difference in cortisol levels between groups ($F(1,9) = 0.87$, $p = 0.38$, partial $\eta^2 = 0.09$), although there was a medium to large effect size. There was a trend for a significant group by time interaction ($F(2,18) = 3.13$, $p = 0.07$, partial $\eta^2 = 0.26$). Peak VO_2 was correlated with cortisol levels at all time points: pre-exercise ($r = 0.92$, $p < 0.001$), 5 min after exercise when cortisol peaked ($r = 0.55$, $p < 0.07$), and 30 min after exercise ($r = 0.72$, $p < 0.01$). The change in cortisol from pre-exercise to 30 min after exercise was inversely associated with pain tolerance 30 min after exercise ($r = –0.62$, $p < 0.05$). When cortisol was normalized by BMI and correlated with pain sensitivity, the results were similar. Specifically, the change in cortisol from pre-exercise to 30 min after exercise was inversely correlated with pain tolerance after exercise ($r = –0.69$, $p < 0.05$).

Dehydroepiandrosterone

Figure 2(b) shows mean DHEA levels by group across the three time points at which it was measured. A repeated-measures ANOVA using age as a covariate and with sphericity assumed showed no significant difference in DHEA levels across time ($F(2,18) = 1.31$, $p = 0.29$, partial $\eta^2 = 0.13$), although there was a large effect size. DHEA levels also were not different between groups ($F(1,9) = 0.80$ $p = 0.39$, partial $\eta^2 = 0.08$), although there was a medium to large effect size. There was a trend for a significant group by time interaction ($F(2,18) = 4.71$, $p = 0.09$, partial $\eta^2 = 0.24$). Peak VO_2 was not correlated with DHEA levels. However, similar to the findings for cortisol, the change in

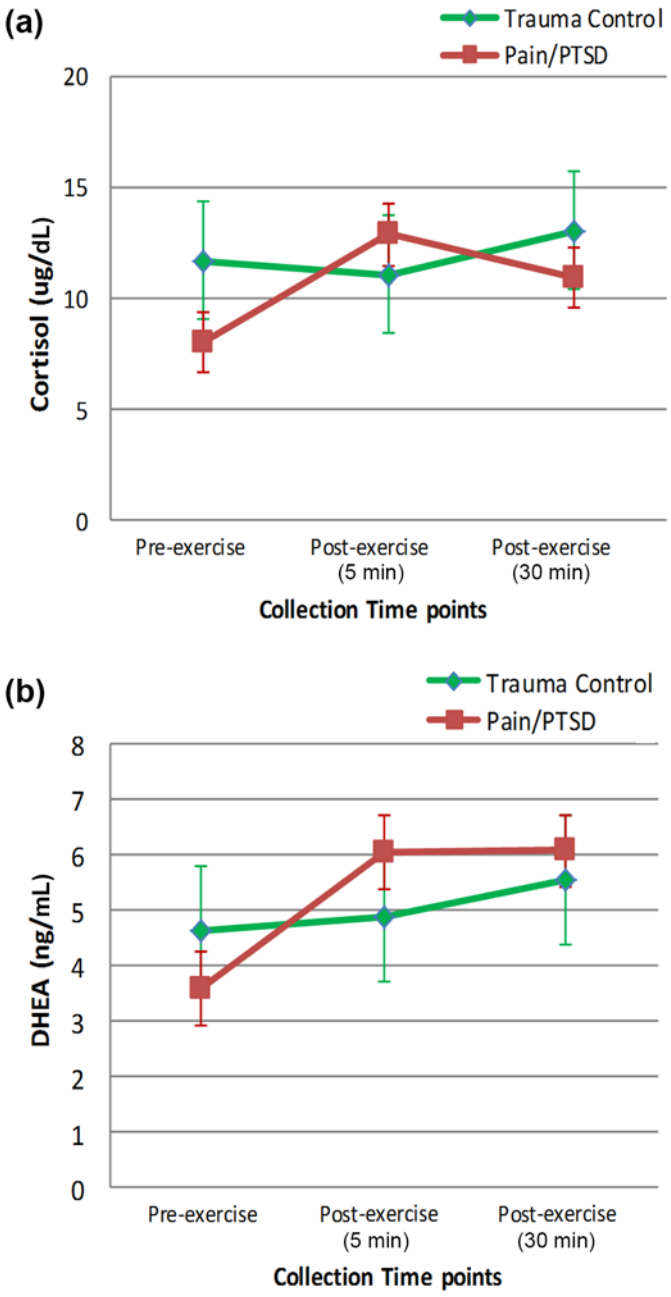

Figure 2.
(a) Plasma cortisol levels and **(b)** plasma dehydroepiandrosterone (DHEA) levels (mean ± standard error) by group across three time points at which they were measured: pre-exercise, 5 min after exercise, and 30 min after exercise. PTSD = post-traumatic stress disorder.

DHEA from pre-exercise to 30 min after exercise was inversely correlated with pain tolerance after exercise ($r = –0.58$, $p < 0.05$). DHEA normalized by BMI also correlated with pain tolerance after exercise ($r = –0.58$, $p < 0.05$).

DISCUSSION

The results of this study demonstrate significant positive correlations between peak VO_2 and baseline, as well as peak, NPY levels suggesting that the capacity for NPY synthesis and release is related to cardiorespiratory fitness. Additionally, the peak change in NPY in response to CPX was significantly correlated with pain threshold after exercise. Across biological systems, NPY is known to raise the threshold for release of neurotransmitters with which it is localized by acting at inhibitory presynaptic NPY-Y_2 receptors [21], suggesting that this mechanism may contribute to its possible acute antinociceptive effects. Effects at upregulated NPY-Y_1 receptors in the spinal cord in response to acute pain are, in turn, thought to prevent progression of acute pain to chronic pain [13].

As previously noted, we expected there to be group differences in NPY baseline and peak levels achieved in response to CPX. However, there was marked individual variability in NPY levels and responses in both groups and no significant differences between groups or across time points in this small pilot sample. According to Morgan et al., genetic influences and degree of trauma exposure, but not necessarily PTSD diagnosis, are related to lower resting levels of NPY [25], but data in the field are yet lacking with regard to the relationships among NPY genetic factors, trauma exposure, PTSD diagnosis, and NPY reactivity to stress. Future work in larger samples will be required to evaluate these issues.

As demonstrated by Pernow et al., exercise at a mean 70 percent of VO_2 peak increases serum NPY in healthy humans [28]. As seen in **Figure 1(a)**, most of the participants in both the chronic pain/PTSD and TC groups (among whom mean fitness was poor) showed only slight increases in plasma NPY from baseline to peak levels measured 5 min after exercise. However, taken together, these findings suggest that even patients with chronic pain/PTSD have the potential to release NPY in response to exercise, with possible effect on pain threshold. Since NPY was correlated with VO_2, an index of cardiorespiratory fitness, we hypothesize that progressive exercise training may further increase the capacity for NPY release in patients with chronic pain/PTSD to potentially reduce pain sensitivity and perhaps also improve PTSD symptoms.

In contrast to the findings for NPY, there were significant progressive increases in ALLO levels across all time points, suggesting that ALLO is released at lower levels of stress intensity. Consistent with work in rodents by Purdy et al. [32], ALLO levels peaked about 60 min after initiation of stressors, later than for the other neurohormones tested. Consistent with the findings for NPY, we did not find significant group differences in ALLO levels in this small pilot sample. Genetic predisposition and possibly trauma exposure may affect resting ALLO levels as well as the capacity for release of ALLO in response to stress. Thus, further longitudinal research will be needed to sort out the relationships among genetic factors, trauma exposure, PTSD, and alterations in ALLO levels and responses.

For all study participants, there was a significant positive correlation between peak VO_2 and the change in ALLO from baseline to 30 min after exercise. Similar to NPY, these findings suggest that the capacity to release ALLO is related to cardiorespiratory fitness. The change in ALLO between baseline and 30 min after exercise was also significantly correlated with pain tolerance after exercise. This finding is consistent with work by Sripada et al. demonstrating reductions in activity of the amygdala and insula, areas central to the experience of pain, in association with experimentally induced increases in plasma levels of allopregnanolone [44]. In addition, allopregnanolone enhanced dorsal medial prefrontal cortex activity and the connectivity between dorsal medial prefrontal cortex and amygdala in association with reductions in anxiety—thus demonstrating a significant role for allopregnanolone in emotion regulation, a construct likely related to pain tolerance.

There were large effect sizes for PTSD/chronic pain versus TC group differences in DHEA and cortisol levels generally, expected medium to large effect sizes for increases in response to exercise for both groups (**Figure 2**), and a trend for increased DHEA responding in the PTSD group, which could in part be related to greater trauma exposure in that group [47–48]. However, for all study participants, acute exercise-induced increases in both cortisol and DHEA were inversely correlated with pain tolerance after exercise. We suggest that possible pharmacological effects of DHEA that counter those of ALLO [15] and direct detrimental effects of cortisol on the balance between prefrontal cortical [49] and amygdala reactivity [50] may underlie this finding.

Finally, it is important to briefly discuss the significant difference found between study groups for BMI. While the pain/PTSD group had a significantly greater mean BMI than the TC group, both groups contained individuals at the high end of the BMI range. This finding is not surprising given that obesity continues to be a significant health problem in the U.S. general population [51]. The pain/PTSD group had a BMI consistent with obesity category III, and most of these participants were Veterans. Among Veterans in Veterans Health Administration care, obesity is more prevalent than for non-Veterans. Multiple morbidities such as pain, PTSD, and obesity are more likely to adversely affect overall health, functioning, and quality of life for these individuals [51–57]. In fact, additional research has focused on the mediating role of trauma exposure or PTSD and related neurobiological factors in adverse health conditions such as metabolic syndrome [56]. Given that exercise is beneficial for the treatment of such adverse health conditions, including chronic pain, the investigation of exercise as a potential multisystem treatment intervention for men and women suffering from chronic pain and PTSD is compelling.

IMPLICATIONS

Restoring normal NPY and ALLO levels and responses to stress could help with the management of chronic pain in a PTSD population. As reviewed by Scioli-Salter et al. [13], pain can trigger memories as well as emotional and physiological reexperiencing of a trauma by activating the amygdala via sensory projections routed through the thalamus and parabrachial nucleus. Activation of the amygdala, in turn, can affect pain sensitivity by increasing molecular substrates in the dorsal horn of the spinal cord that facilitate transmission of pain from the periphery. Thus, trauma cues or pain experiences that activate the amygdala may progressively intensify the simultaneous experience of PTSD reexperiencing symptoms and peripheral pain. Thus, neurobiological factors, such as NPY and ALLO that both diminish the reactivity of the amygdala and directly diminish pain transmission in the spinal cord, may reduce both pain sensitivity and PTSD symptoms. In fact, when hyperreactivity of the amygdala is diminished, frontal lobe function and frontal lobe inhibition of the amygdala also improve. This may further enhance pain tolerance and allow for higher-order cognitive processing, which may, in turn, promote recovery from traumatic stress.

Therefore, given our observation of the strong relationship between fitness and exercise-induced increases in NPY

and ALLO, we hypothesize that exercise training could complement and improve the efficacy of cognitive-based treatments for both chronic pain and PTSD by increasing the capacity for release of these molecules. This is supported by recent work showing that 2 wk of moderate aerobic exercise training in already fit male rowers further increased the capacity for NPY release in response to a subsequent acute exercise challenge [29]. In addition, exercise has been shown to enhance vagal parasympathetic neurotransmission and thereby suppress proinflammatory pathways—another pathway by which chronic pain might be improved. Furthermore, progressive exercise training focused on reaching biological targets such as raising plasma levels of NPY and ALLO may help to break the vicious circle between pain and pain-avoidance behaviors (including avoidance of exercise). Exercise-related reductions in pain and perhaps reestablishment of exercise-induced reward potentially mediated by NPY [57–59] may also serve to enhance intrinsic motivation and maintenance of exercise.

CONCLUSIONS

Our pilot work in trauma-exposed individuals with and without PTSD/chronic pain shows a strong, positive relationship between postexercise pain threshold and plasma NPY and between pain tolerance and ALLO levels and responses, as well as a strong, inverse relationship between pain tolerance and exercise-induced changes in plasma cortisol and DHEA levels. Exercise-related changes in these neurohormones were also related to cardiorespiratory fitness. These pilot study findings thus suggest that progressive exercise training could potentially increase the capacity for release of NPY and ALLO in response to exercise challenge, if not in response to stress more generally, and thereby reduce pain sensitivity in a chronic pain and PTSD population. We are currently testing these hypotheses using symptom-limited CPX before and after a 12 wk individualized progressive exercise training program in trauma-exposed Veterans with and without chronic pain/PTSD. Defining the biology underlying exercise-related improvements in pain in populations with chronic pain and PTSD may help optimize implementation of exercise programs for this population, as well as guide development of other novel pharmacological and nonpharmacological therapies to reduce suffering and disability in this population.

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Opioid use and walking among patients with chronic low back pain

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Abstract—This study examined the effect of a walking intervention on step counts among patients with chronic back pain who report opioid use. Data were collected as part of a randomized trial to reduce back-pain-related disability. Participants (n = 118 usual care, 111 intervention) were Veterans receiving care within one healthcare system. Step counts were collected at baseline, 6 mo, and 12 mo via an uploading pedometer. Self-reported opioid use was collected by survey. More than 40% (n = 99) of participants reported opioid use at baseline. After adjustment, the predicted mean step count for baseline opioid users assigned to the intervention increased by more than 1,200 steps compared with a reduction of nearly 400 steps for those assigned to usual care (between-group difference = 1,625 steps, p = 0.004). Among nonopioid users, there was no change for those in the intervention (–16 steps) and an increase of about 660 steps for those assigned to usual care (between-group difference = 683 steps, p = 0.17). These data show that patients taking opioids may engage in walking to help manage their back pain. This finding emphasizes the importance of encouraging the use of alternative pain management strategies for these patients.

Clinical Trial Registration: ClinicalTrials.gov; "Veterans Walk to Beat Back Pain": NCT00694018; https://clinicaltrials.gov/ct2/show/NCT00694018

Key words: chronic back pain, exercise therapy, objective measurement, opioids, pain management, pain-related disability, pedometer, step counts, Veterans, walking.

INTRODUCTION

Managing chronic low back pain is a major public health and clinical challenge [1–4]. This challenge may be even more prominent within the Department of Veterans Affairs (VA) healthcare system, given that back pain is highly prevalent among VA general medicine patients and a chief complaint for Veterans who have returned from the conflicts in Iraq and Afghanistan [5–7]. Low back pain clinical guidelines recommend use of various self-care options, medications, and nonpharmacologic strategies, such as cognitive behavioral therapy or exercise therapy, when self-care alone does not lead to improvement [8]. However, the delivery of optimal back pain care appears to be an elusive goal [9–10].

An analysis of spine care in the United States showed that between 1999 and 2010 the use of guideline-concordant treatments, such as physical therapy or nonopioid medications (e.g., nonsteroidal anti-inflammatory drugs

Abbreviations: CES-D 10 = Center for Epidemiologic Studies Depression Scale, NSAID = nonsteroidal anti-inflammatory drug, RDQ = Roland and Morris Back Pain Disability Questionnaire, VA = Department of Veterans Affairs.

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[NSAIDs]), has remained stable or decreased [9]. On the other hand, the use of non-guideline-concordant therapy, such as advanced imaging and opioids, appears to be increasing [9]. Likewise, studies have found generally low use of nonpharmacologic therapies in clinical practice [2], while medications, including opioids, are commonly used for treating chronic back pain [2,11–12]. The use of opioids for chronic back pain is especially concerning given well-documented problems with safety and effectiveness, particularly with longer term use [3,11–16].

A recent Cochrane review identified randomized controlled trial evidence of short-term benefits with opioids versus placebo in reducing pain and improving function for individuals with chronic low back pain [14,17]. There are few studies, however, and no evidence that opioids are better than NSAIDs or antidepressants for addressing either pain or function and no data on the use of opioids for managing chronic back pain beyond 4 mo [17–18]. Whether patients receiving longer term opioid therapy can or will engage in physical activity, a recommended approach for managing chronic back pain [8,19–20], is also unknown. The purpose of this study, therefore, was to assess whether Veterans with chronic back pain, and particularly those who report opioid use, are willing to engage in physical activity by examining the effect of a walking intervention on objectively measured step counts.

METHODS

Study Population and Data Collection

Data were collected as part of a randomized controlled trial of a pedometer-based, Internet-mediated intervention to promote walking as a form of exercise therapy and reduce back-pain-related disability. The design, rationale, and main results for the primary study are described in detail elsewhere [21–22]. Briefly, we recruited patients with back pain from one VA healthcare system. Specific eligibility criteria included: (1) persistent back pain >3 mo, (2) sedentary lifestyle (<150 min of physical activity per week), (3) weekly access to a computer with a USB port and Internet access, (4) ability to provide consent and communicate in English, (5) community residence, (6) ability to walk at least one block; and (7) self-report not currently pregnant. After attending a single-session back class led by a physical therapist, all potential participants received an enhanced pedometer, Omron HJ-720ITC (Omron Healthcare, Inc; Lake Forest, Illinois), which contains a dual axial accelerometer, stores 42 d of step count data, and has an embedded USB port [23]. Participants were instructed to wear the pedometer for 7 d with the step count display covered, allowing us to obtain a baseline measurement. After we received 7 d of valid pedometer data and a completed baseline survey, we randomized 229 participants, with 118 allocated to receive enhanced usual care (control group) and 111 allocated to receive the full intervention. The study protocol was approved by the VA Ann Arbor Healthcare System Institutional Review Board, with written informed consent obtained for all participants.

Results from the primary study showed that compared with participants receiving usual care, intervention participants reported a greater decrease in back-pain-related disability in the 6 mo following study enrollment, but the difference between groups was no longer significant at 12 mo [22]. The primary components of the intervention included (1) individualized step count goals, which participants received weekly via email; (2) feedback on progress toward meeting step count goals provided through a study Web site; (3) targeted educational and motivational messages posted on the Web site (e.g., tools for positive thinking, walking for your mind and spirit); and (4) social support provided through an asynchronous electronic forum accessed through the study Web site (i.e., an area on the Web site where intervention participants and research staff could share success stories, make suggestions, or ask questions). The weekly step goal email messages also served as a reminder for those in the intervention to upload their pedometer data. Usual care participants received a monthly email-based upload reminder. Reminders were also sent to all participants at 6 and 12 mo asking them to upload their pedometer data and complete an online study survey. The uploaded pedometer data along with the survey data collected at baseline, 6 mo, and 12 mo are the primary data sources for this study, although some data on opioid use were also obtained from VA electronic medical records.

Study Measures

The primary outcome was change in daily step counts. Step counts were measured as the average number of steps per day over the previous 7 d using step count data collected through pedometer uploads at baseline, 6 mo, and 12 mo. The change in daily steps was calculated by subtracting baseline step counts from step counts at 6 and 12 mo.

The principal independent variables were binary indicators of self-reported opioid use at baseline and assigned study group (intervention or usual care). Specifically, study participants who responded "yes" to the following question on the baseline survey: "Do you take a narcotic medication for pain relief?" (examples of narcotics include codeine, Tylenol® No. 3 with codeine, hydrocodone, Vicodin®, hydromorphone, methadone, morphine, oxycodone, and Percocet®) were classified as using opioids. We used patient self-report as our primary measure of opioid use, given that some patients may obtain their medication outside of the VA system. However, prescription data from VA electronic pharmacy records were used to confirm our self-report classification as well as determine the receipt of opioid medications at 6 and 12 mo.

Other baseline variables included age, sex, race, body mass index, and the Center for Epidemiologic Studies Depression Scale (CES-D 10) [24]. Pain severity was evaluated using a numeric rating scale (0 = "no pain" and 10 = "worst pain imaginable") [25], while back-pain-related disability, the primary outcome for the trial, was measured using the Roland and Morris Back Pain Disability Questionnaire (RDQ) [26], a 24-item scale with higher scores indicating greater disability. Both pain severity and back-pain-related disability were assessed at all three time points along with a self-efficacy for exercise measure, based on the Exercise Regularly Scale [27]. Study participants were also asked about the use of healthcare services during the past 6 mo, including the number of visits to a doctor's office or clinic and the receipt of physical therapy and injections to help manage pain.

Statistical Analysis

We used *t*-tests and chi-square tests to compare the characteristics of participants who reported taking opioid medications at baseline versus those who did not. Differences in step counts, pain-related outcomes, and opioid use between intervention and control participants within opioid use subgroups were also assessed using *t*-tests and chi-square tests. The data were then analyzed using a linear mixed-effects model with the difference in daily steps from baseline at both 6 and 12 mo as the dependent variables. The independent variables consisted of the baseline daily step count, an indicator variable for opioid use at baseline, an indicator for intervention group, and an interaction term of opioid use at baseline by intervention group. The model also included baseline values for age, sex, body mass index, level of pain severity, RDQ score, exercise self-efficacy score, CES-D 10 Score, received injections, received physical therapy, and number of outpatient visits in the prior 6 mo. An indicator for assessment time (e.g., 12 mo) was also included, and each participant's data was modeled using random intercepts to account for within-patient correlation of the repeated measures. Step count changes were reported based on the predicted or marginal means generated by the model for the intervention and control participants within opioid use subgroups. All analyses were conducted using Stata/MP 13.1 (Stata Corp; College Station, Texas). Statistical tests were two-tailed, with $p < 0.05$ considered statistically significant.

Because of missing pedometer data at both 6 and 12 mo, as some participants were unable to or did not upload the information, we also conducted our analysis using multiple imputation. Specifically, at 6 mo, 38 participants (38%) in the baseline opioid use group and 34 (28%) in the no opioid use group were missing pedometer data; at 12 mo, 41 participants (41%) in the opioid use group and 40 (33%) in the no opioid use group were missing data. To account for missing covariates as well as missing outcomes, we created five imputed data sets by an iterative multivariable regression technique using all available baseline covariates we suspected to be relevant to the missing data mechanism, including baseline demographic variables, intervention group status, opioid use status, and follow-up outcomes. Across the imputed data sets, the estimates were combined using Rubin's combining rules [28]. Since the directionality, magnitude, and statistical significance of our primary findings persisted, we present only the results from the nonimputed analysis.

RESULTS

At baseline, more than 40 percent (99/229) of participants reported using opioid medications for pain management. Only 8 participants did not self-report their opioid use status at baseline. Participant opioid use was confirmed through VA prescription data, with 83 percent of those who reported opioid use filling a prescription for an opioid medication in the prior 100 d compared with 7 percent of those who reported no opioid use (**Table 1**). Moreover, among self-reported opioid users, a majority (68%) had evidence of longer term use, defined as ≥16 wk [29]. The most frequently filled medications were hydrocodone-acetaminophen products followed by oxycodone or oxycodone-acetaminophen medications. There were no baseline differences between those using and not using opioids with

Table 1.
Baseline characteristics for those reporting opioid use versus no opioid use. Data presented as *n* (%) or mean ± standard deviation.

Variable	Opioid Use Reported at Baseline (*n* = 99)*	No Opioid Use Reported at Baseline (*n* = 122)*	*p*-Value
Age, yr	52.7 ± 10.1	50.3 ± 14.4	0.15
Male	88 (89)	105 (86)	0.53
White	80 (81)	98 (80)	0.93
Body Mass Index	31.3 ± 5.5	30.8 ± 5.6	0.53
Level of Pain Severity (0–10)	6.3 ± 1.7	5.8 ± 1.8	0.02
RDQ Score (0–24)	10.5 ± 5.9	8.6 ± 5.5	0.02
Exercise Self-Efficacy Score	6.1 ± 2.2	7.1 ± 2.2	0.001
Depression Score	14.8 ± 6.1	11.6 ± 6.6	<0.001
No. Outpatient Visits in Past 6 mo	10.3 (12.1)	9.1 (11.3)	0.45
Received Injections in Past 6 mo	21 (21)	10 (8)	0.006
Received Physical Therapy in Past 6 mo	39 (39)	44 (36)	0.61
In Intervention Group	44 (44)	64 (52)	0.24
VA Fill for Opioid Medication in Prior 100 d	82 (83)	8 (7)	<0.001
Baseline Daily Step Counts	4,005.4 ± 2,131.3	4,811.3 ± 2,770.8	0.02

*n = 8 missing/did not respond to opioid use question.
RDQ = Roland and Morris Back Pain Disability Questionnaire, VA = Department of Veterans Affairs.

respect to age, sex, race, body mass index, or number of outpatient visits in the prior 6 mo (**Table 1**). There was also no significant difference in the proportion of participants randomized to the study intervention group between those with and without reported opioid use. However, participants who reported using opioids at baseline had higher reported pain levels (6.3 vs 5.8, $p = 0.02$), higher back-pain-related disability scores (10.5 vs 8.6, $p = 0.02$), a higher reported level of depressive symptoms (14.8 vs 11.6, $p < 0.001$), and lower exercise self-efficacy scores (6.1 vs 7.1, $p = 0.001$) than those with no reported opioid use. A higher percentage of opioid users also reported that they were receiving injections to help manage their back pain (21% vs 8%, $p = 0.006$).

Average daily step counts were significantly lower for opioid users compared with nonusers at baseline (4,005.4 vs 4,811.3, $p = 0.02$). Likewise, average daily step counts remained lower at 6 mo (4,823.0 vs 5,242.2, $p = 0.42$) and 12 mo (4,599.3 vs 4,881.1, $p = 0.59$) for those participants who reported using opioid medications at baseline compared with those who did not. However, after taking into account assigned study group (intervention vs usual care), unadjusted changes in average daily steps were substantially greater at both 6 and 12 mo among those who reported opioid use at baseline who were assigned to the intervention (**Table 2**). At 6 mo, step counts for opioid users in the intervention group increased by more than 1,400 steps from baseline, compared with a decrease of about 150 steps in those assigned to usual care (between-group difference = 1,632 steps, $p = 0.03$). In the nonopioid group, both intervention and usual care participants had relatively modest increases in their step counts, but the changes were not significantly different (between-group difference = 309 steps, $p = 0.68$). Similarly, at 12 mo, average step counts among baseline opioid users in the intervention were more than 1,000 steps higher than their baseline step counts, while those in the usual care group were more than 200 steps lower (between-group difference = 1,305 steps, $p = 0.05$); the changes for study participants with no reported opioid use were again not statistically different (between-group difference = 513 steps, $p = 0.31$).

Results from the linear mixed-effects model, as shown by the adjusted predicted mean difference in daily steps for each group averaged across the two follow-up times at 6 and 12 mo (**Figure**) are generally consistent with the unadjusted findings. After adjustment, among participants with reported opioid use at baseline, the predicted mean increase for those assigned to the intervention group was more than 1,200 steps over the two follow-up time points, as compared with a reduction of nearly 400 steps for those assigned to the usual care group (between-group difference = 1,625 steps, $p = 0.004$). Among nonopioid users, there was essentially no change in step counts in the intervention group and an increase of about 660 steps in the usual care group

Table 2.
Unadjusted changes in steps, pain, function, and opioid fills by baseline opioid use and intervention group. Data presented as *n* (%) or mean ± standard deviation.

Variable	Reported Opioid Use			No Reported Opioid Use		
	Intervention (*n* = 44)	Usual Care (*n* = 55)	*p*-Value	Intervention (*n* = 64)	Usual Care (*n* = 58)	*p*-Value
Daily Step Counts						
Baseline	4,069.7 ± 2,583.1	3,953.0 ± 1,701.0	0.79	4,858.1 ± 2,865.1	4,760.4 ± 2,688.6	0.85
Difference (6 mo)*†	1,478.9 ± 3,833.0	−153.5 ± 1,599.7	0.03	400.2 ± 3,182.6	91.7 ± 3,760.6	0.68
Difference (12 mo)*†	1,087.4 ± 2,889.6	−218.0 ± 1,935.3	0.05	−359.0 ± 2,519.4	154.3 ± 1,861.1	0.31
Pain Severity (0–10)						
Baseline	6.5 ± 1.6	6.2 ± 1.7	0.41	5.7 ± 1.9	5.9 ± 1.6	0.37
Difference (6 mo)*†	−1.0 ± 2.1	−0.43 ± 1.7	0.14	−1.4 ± 2.0	−1.1 ± 1.7	0.51
Difference (12 mo)*†	−0.31 ± 1.5	−0.18 ± 1.8	0.72	−0.67 ± 2.1	−0.86 ± 1.6	0.61
RDQ Score (0–24)						
Baseline	10.4 ± 5.5	10.5 ± 6.2	0.91	8.2 ± 5.9	9.1 ± 5.1	0.37
Difference (6 mo)*†	−1.3 ± 6.1	0.46 ± 4.5	0.13	−2.2 ± 5.6	−1.5 ± 4.7	0.51
Difference (12 mo)*†	−2.6 ± 7.8	−1.2 ± 6.8	0.39	−1.6 ± 5.7	−1.6 ± 5.0	0.93
VA Fill for Opioid Medication in Prior 100 d						
Baseline	35/44 (80)	47/54 (87)	0.32	5/63 (8)	3/57 (5)	0.56
6 mo	24/43 (56)	34/54 (63)	0.48	8/60 (13)	11/55 (20)	0.35
12 mo	21/43 (49)	29/54 (54)	0.63	10/59 (17)	10/55 (18)	0.86

Note: *p*-values are based on *t*-tests or chi-square tests.
*All differences are calculated as follow-up minus baseline values, so negative values for pain severity and RDQ score indicate improvement.
†Number of subjects in each group varies over time due to nonresponse or loss to follow-up. Difference in daily step counts: among opioid users *n* = 30 intervention, *n* = 31 usual care at 6 mo and *n* = 30 intervention, *n* = 28 usual care at 12 mo; among nonopioid users *n* = 51 intervention, *n* = 36 usual care at 6 mo and *n* = 46 intervention, *n* = 36 usual care at 12 mo. Difference in survey derived measures (pain severity and RDQ score): among opioid users *n* = 40 intervention, *n* = 51 usual care at 6 mo and *n* = 39 intervention, *n* = 50 usual care at 12 mo; among nonopioid users *n* = 58 intervention, *n* = 50 usual care at 6 mo and *n* = 59 intervention, *n* = 49 usual care at 12 mo.
RDQ = Roland and Morris Back Pain Disability Questionnaire, VA = Department of Veterans Affairs.

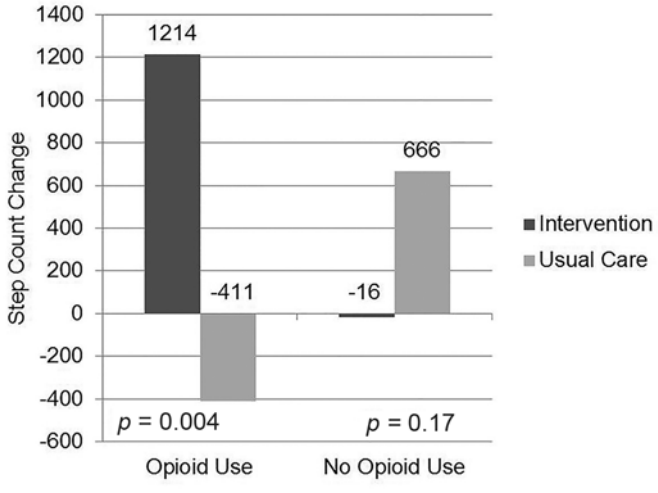

Figure.
Six and twelve month adjusted average change in daily step counts from baseline by group.

(between-group difference = 683 steps, $p = 0.17$). The results after use of multiple imputations to account for missing data were similar (results not shown).

Table 2 shows unadjusted changes in pain severity, back-pain-related functional disability, and fills for opioid medications by study group at each time point. Most changes, in general, reflected improvements over time. Although not statistically significant, level of pain severity at 6 and 12 mo was lower for all of the study groups, with a larger reduction at 6 mo than at 12 mo. Except for those patients on opioids at baseline and in the usual care group who had an increase in average disability scores at 6 mo (by about 1/2 a point), all other patient subgroups reported less back-pain-related disability (lower RDQ scores) at both time points, with the greatest improvement reported by baseline opioid users in the intervention group at 12 mo (a difference of –2.6 from baseline). The percentage of patients with VA fills for opioid medications declined over time among those with reported opioid use

at baseline and increased slightly among the nonopioid users. However, the patterns in reported use (and opioid dose as shown in the **Appendix** [available online only]) were similar between intervention and usual care participants within each subgroup.

DISCUSSION

Managing chronic back pain is a significant challenge in the United States and worldwide [1,9]. Efforts to improve management of this prevalent condition are growing, fueled by concerns about the potential overuse and risks associated with opioid medications, coupled with the apparent underuse of other recommended options, such as exercise therapy and nonopioid medications [2,8–9,30]. To inform these efforts, we examined the effect of a walking intervention on average daily step counts among Veterans with chronic back pain that did and did not report opioid use. Our findings revealed a notable increase (>1,000 steps or approximately 1/2 mile a day) over the two follow-up time periods among study participants who were using opioids at baseline and who were assigned to the intervention group.

Specific reasons for this increase in walking activity are unknown but could be due in part to better pain relief and improved exercise tolerance. Indeed, this marked increase was not observed for intervention patients who did not report opioid use at baseline. In addition to studies that show improvements in measured exercise performance following acute opioid use [31–32], a multicenter study by Teske et al. [33] found that controlled-release oxycodone helped patients with movement pain engage in physical therapy. In our study, reported pain severity was lower at 6 and 12 mo compared with baseline for those who used opioids at baseline and who were assigned to the intervention group. Reductions in pain severity were also reported by other study participants; thus, the extent to which pain control might be related to the increased step counts is unclear. Nonetheless, this potential association between opioid use and objectively measured exercise performance, including specific mechanisms of action, such as pain reduction or increased tolerance, warrants additional study. Why the intervention appeared to be particularly helpful in increasing step counts among opioid users compared with nonopioid users is also a topic for further investigation.

Increased step counts, as a measure of function, are an important outcome in their own right. However, whether this increased activity is related to improvements in other important pain-related outcomes is also of interest. In general, our analysis showed a reduction in pain severity and back-pain-related disability over time across all study groups. Although there were no statistically significant differences within subgroups at 6 or 12 mo, participants with reported opioid use at baseline assigned to usual care had the least amount of improvement compared with the other groups. Some changes in VA opioid medication fills were also observed. Similar patterns, however, were observed in both the intervention and usual care groups and thus do not suggest any specific benefits related to the increase in steps found among the opioid users in the intervention group.

Perhaps one of the most important findings from this analysis is that patients receiving opioids were both willing and able to engage in walking to help manage their back pain, particularly when provided with additional support. Participants who reported opioid use at baseline and were assigned to the usual care group had basically no change in step counts during the 12 mo study period. Those assigned to the intervention, who received support in the form of walking goals, performance feedback, motivational messages, and social support, on the other hand, had a substantial increase that persisted over time. All too often clinicians may view patients who are on opioids as more recalcitrant and unlikely to use other pain management modalities. Similar to work by Fleming et al. [34], who found that complementary and alternative medicine was widely used by opioid users, our results show that opioid users may use walking to manage their back pain. This finding emphasizes the importance of supporting the use of alternative pain management strategies for patients with chronic back pain who are receiving opioids.

This study has some limitations. First, this is a secondary analysis of data collected as part of a randomized controlled trial. The interaction between baseline opioid use and the intervention was not a prespecified analysis and the study was not powered for a subgroup analysis of pain-related outcomes or service utilization. Nonetheless, we believe this is an important finding and warranted additional, even if somewhat preliminary, investigation. Second, there is a substantial amount of missing step count data. While this is a significant limitation, having objectively measured information on physical activity is

also a strength given the inherent unreliability of subjectively reported measures [35]. In addition, confidence in our main finding is enhanced through our use of multiple imputation procedures. Third, although the study sample consisted only of Veterans, we have no specific reason to suspect that the results would be substantially different with a non-Veteran population.

CONCLUSIONS

These limitations notwithstanding, our findings are important in the continuing quest for effective and safe treatment of chronic back pain. Our results suggest that use of opioid medications for chronic back pain could facilitate participation in walking as a form of exercise therapy, although this potential benefit must be balanced against the documented risks of opioid use. More importantly, these data show that patients receiving opioids may engage in walking to help manage their back pain when provided with additional support. Although more work is needed to determine the exact mechanisms of action and potential benefits associated with opioid use and walking as a form of exercise therapy, this study reinforces the importance of supporting the use of alternative pain management strategies for patients with chronic back pain who are receiving opioids.

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Perceptions of other integrative health therapies by Veterans with pain who are receiving massage

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Abstract—Veterans are increasingly using complementary and integrative health (CIH) therapies to manage chronic pain and other troubling symptoms that significantly impair health and quality of life. The Department of Veterans Affairs (VA) is exploring ways to meet the demand for access to CIH, but little is known about Veterans' perceptions of the VA's efforts. To address this knowledge gap, we conducted interviews of 15 inpatients, 8 receiving palliative care, and 15 outpatients receiving CIH in the VA. Pain was the precipitating factor in all participants' experience. Participants were asked about their experience in the VA and their opinions about which therapies would most benefit other Veterans. Participants reported that massage was well-received and resulted in decreased pain, increased mobility, and decreased opioid use. Major challenges were the high ratio of patients to CIH providers, the difficulty in receiving CIH from fee-based CIH providers outside of the VA, cost issues, and the role of administrative decisions in the uneven deployment of CIH across the VA. If the VA is to meet its goal of offering personalized, proactive, patient-centered care nationwide then it must receive support from Congress while considering Veterans' goals and concerns to ensure that the expanded provision of CIH improves outcomes.

Key words: access, complementary and alternative medicine, cost, inpatients, integrative health, massage therapy, mobility, opioid use, outpatient, pain, patient to provider ratio, patient-centered care, Veterans.

INTRODUCTION

Like millions of Americans, Veterans are using complementary and integrative health (CIH) therapies such as massage and acupuncture and/or practicing CIH self-care activities like yoga, Qigong, Tai Chi, and meditation [1]. The Veteran's goal is to find new approaches to managing and/or rehabilitating from chronic pain, anxiety, posttraumatic stress disorder (PTSD), and other troubling symptoms, which significantly affect health and quality of life. Research on many of these therapies has shown promising results [2–8]. The Department of Veterans Affairs (VA) is exploring ways to meet this demand for access to CIH when combined with conventional medical care. In 2010, the VA created the Office of Patient Centered Care and Cultural Transformation. Included in the office's responsibilities is the promotion of CIH within the VA through the recent establishment of an Integrated Health Coordinating Center [9].

Although there is increasing research about the use of CIH therapies in the VA [10–17], less is known about how Veterans perceive these therapies. In a study of 401 Veterans with non-cancer-related chronic pain, Denneson et al. found that 96.8 percent were willing to try massage therapy [1]. We theorized that patients whom we

Abbreviations: CIH = complementary and integrative health, PTSD = posttraumatic stress disorder, VA = Department of Veterans Affairs.

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were studying quantitatively related to massage therapy might also be open to discussing other CIH therapies. The purpose of this qualitative portion of our study was to examine the experience, knowledge, and opinions of Veterans receiving massage therapy at a large VA facility regarding massage therapy in particular and CIH therapies in general.

METHODS

We conducted a mixed-methods pilot study at one VA site as part of a study funded by the National Center for Complementary and Alternative Medicine of the National Institutes of Health. The aim of a supplement to the parent study was promotion of a collaboration between a non-VA hospital with an extensive CIH program and a VA hospital for the purpose of promoting CIH at the VA site [18–19]. To better understand how CIH was currently viewed at the VA, our approach included interviews of VA patients, providers, and administrators about the use of CIH.

Participants

The results of the interviews with providers and administrators have been previously published [20]. For the portion of the study reported here, a convenience sample of 30 participants was recruited for qualitative interviews, including 15 inpatients and 15 outpatients. The inpatients were approached by the research assistant regarding study participation prior to receiving a therapeutic massage. The outpatients were approached when they came for their massage appointments. For some inpatients, the interview occurred at the time of their first massage. All participants were receiving or had received therapeutic massage at the VA as part of their treatment for chronic pain or as part of their palliative care including pain relief.

Data Collection

During the study period, the therapist received 129 referrals from VA providers for provision of therapeutic massage services. Of the 84 inpatient referrals, 65 were on the palliative care service. Of the 45 outpatient referrals, 23 were receiving palliative care and 22 were primary care patients diagnosed with a chronic pain condition. From these referrals, 15 inpatients (based on willingness and ability to communicate; many were too ill) and 15 outpatients (based on willingness and availability to participate) were interviewed. Subjects described their experience with CIH therapies (including those services experienced outside of the VA) in general and with massage in particular, their views about the use of CIH in the VA, and their opinions about which CIH therapies would be most acceptable and/or useful to Veterans. After the participant signed an informed consent form, interviews were conducted and digitally recorded in a private location by one member of the research team (C.E.F.) between May 2013 and May 2014. All participants were asked the same open-ended questions (**Figure 1**), which focused on massage because having received a therapeutic massage was the common denominator in this sample. However, participants were encouraged to discuss use of other CIH therapies as well. Length of the interview ranged from

1. In what ways, if any, did massage therapy change your level of pain and mobility? How did it make you feel?
2. What, if anything, did you like about the massage therapy?
3. What, if anything, did you dislike about the massage therapy?
4. There are many types of therapy that people use on their own without a doctor's prescription. These are called complementary or alternative therapies. In the past, have you or anyone that you know used any other types of these therapies such as acupuncture, healing touch, aroma therapy, herbs, yoga, meditation, chiropractic, or hypnosis? If yes, please describe when, how often, why, and whether it was helpful?
5. Would you like to have the VA offer other types of therapy besides massage? If yes, please look at this list* and tell me which ones would you be most likely to use and why?
6. Is there anything else that you would like to tell me about massage or other complementary therapies? If yes, please feel free to do so.

Figure 1.
Interview questions for patients. *List of some of more common complementary and integrative health therapies. VA = Department of Veterans Affairs.

3:02 to 19:15 min for inpatients and from 7:58 to 29:19 min for outpatients depending on participant responses.

Analysis

Interviews were transcribed verbatim by one team member (E.L.T.). Because the interviewer was familiar with the content of all of the interviews, she developed a list of initial codes to start the review process. Three team members with qualitative experience then individually coded all of the interviews and a fourth team member coded four of them. Using content analysis, the team then met as a group to collaboratively confirm codes and categories [21] using NVivo software (QSR International Pty Ltd; Doncaster, Australia). Emerging themes in the data were identified through extensive discussion and thematic analysis. As new categories emerged, coding was focused and additional codes and subcodes were developed until all reviewers agreed that the essence of the interviews had been captured [21].

RESULTS

The majority of the inpatients was on the palliative care service, male, Caucasian, and age ≥61 yr (average age: 62.3 yr). All outpatients were ambulatory and receiving therapeutic massages to relieve chronic pain. Although one outpatient had been given <1 yr to live due to cancer, the others had no known terminal illnesses. As with the inpatients, most outpatients were Caucasian males evenly divided between ages 41 to 60 and ≥61 yr. **Table 1** summarizes the participant demographics. The participants' responses reported next are categorized under the general headings of experience, knowledge, and opinions.

Experience

With Other Complementary and Integrative Health Therapies

Although the common factor among participants was their experience with therapeutic massage provided in the VA, they had used a wide range of other CIH therapies as well, both within and outside of the VA. After being shown a list of common CIH therapies to stimulate their thinking, each of the participants was asked two questions regarding what CIH therapy or therapies they had personally used and what CIH therapies they would recommend for the VA to promote or initiate for Veterans in general (**Figure 1**). Participants' answers included not

Table 1.
Demographics of interviewed patient population. Data presented as mean ± standard deviation or *n* (%).

Demographic	Inpatient (*n* = 15)	Outpatient (*n* = 15)	Total (*n* = 30)
Age (yr)*	62.3 ± 11.9	61.0 ± 8.9	61.6 ± 10.4
≤40	1 (7)	0 (0)	1 (3)
41–60	4 (27)	7 (47)	11 (37)
≥61	10 (67)	8 (53)	18 (60)
Sex			
Male	14 (93)	13 (87)	27 (90)
Female	1 (7)	2 (13)	3 (10)
Race			
Caucasian	13 (87)	15 (100)	28 (93)
African American	2 (13)	0 (0)	2 (7)
Referring Service†			
Palliative Care	8 (53)	1 (7)	9 (30)
Manual Medicine	3 (20)	11 (73)	14 (47)
Pain Clinic	2 (13)	2 (13)	4 (13)
Rehabilitation	1 (7)	0 (0)	1 (3)
Inpatient Medicine	1 (7)	0 (0)	1 (3)
Using Opioids*	12 (80)	9 (60)	21 (70)

*At time of study enrollment.
†Medical records of one outpatient contained no information about service referring to massage therapy but participant was likely referred by family member.

only the therapies on the list but also items such as transcutaneous electrical nerve stimulation units that are not necessarily considered CIH therapy but that the respondent thought should be included in the grouping. Their personal experiences with CIH were also not necessarily formal but nonetheless informed the participants' definitions of CIH. For instance, when asked whether he practiced meditation one participant stated, "Yes, because you can do a lot of thinking when you are fishing." As it turned out, the outpatients had experienced a broader range of therapies. All (n = 15) had experienced therapeutic massage followed by manual manipulation (osteopathic manipulative treatment available at this particular VA) (n = 10), diet/herbal (n = 9), pet therapy (n = 9), meditation (n = 8), and chiropractic (n = 8). On the inpatient side, all but one participant had experienced therapeutic massage (n = 14), followed by meditation (n = 6), chiropractic (n = 5), and pet therapy (n = 5).

Pain

Pain was the common factor precipitating use of CIH in all of the participants' experiences. Pain experienced by outpatients was largely musculoskeletal, occurring in the back, neck, shoulders, hips, and knees. One participant explained, "The pain level sometimes is so distracting that it debilitates you to the point you cannot function or think straight." Almost all participants described at least a temporarily significant reduction in their level of pain. Massage was described as "taking the edge off," helping manage and mitigate pain. "It doesn't make it go away permanently but it does make you feel better for a while, which when you are in pain all the time is a big thing."

Both inpatients and outpatients reported a decrease in pain from 1 to 3 points on a 0 to 10 numeric rating scale, which is consistent with the scientific literature of CIH on pain for civilian inpatients [18–19]. Reported pain changes were comparable across groups, with the exception that inpatients reported a shorter duration of pain relief than outpatients. This difference may have been due to the causes of inpatient pain, e.g., radiation-induced oral mucositis or pressure from expanding soft tissue tumors. Although a palliative care patient stated that massage did nothing for his pain, he did report that massage calmed him down, an important effect regarding anxiety control. Another described the relief as temporary, adding, "It's too bad that it's not permanent, but it does give me an amount of relief." Another appreciated that it made him feel "real good" even though simply swallowing liquids made the pain start "shooting back." And another described the massage as getting rid of his back pain in "a little bit," but then added, "I enjoyed it; that's for damn sure."

Some outpatients reported a longer-term reduction in pain than inpatients, anything from days to weeks to indefinite relief. A Veteran who now walks independently described being weaned off fentanyl through the combined efforts of a pharmacist, manual medicine provider, and massage therapist. Another stated, "I'd still be walking with a cane and wearing a back brace." A third said he had been able to stop using a walker for the past 2 to 3 yr. All of these participants attributed their improvement to the effects of therapeutic massage.

Massage

Participants reported an overwhelmingly positive response to the therapeutic massages, chiefly as a way to relieve pain but also to increase mobility and flexibility; promote relaxation; foster more restful sleep; and reduce anxiety, stress, depression, and fatigue. Some participants reported an initial increase in pain associated with the depth of the massage, but all felt the end result justified the experience. "She really works my muscles and it's painful, but I always feel better before leaving."

Access

Participants described several separate but interrelated problems regarding access to CIH services. A primary concern was the ratio of providers to patients. This particular VA facility has one massage therapist on staff (almost all other VA hospitals do not have any massage therapists) and one manual medicine practitioner. However, the demand for their services far outstrips what these two providers can provide. As a result, only a limited number of outpatients are offered therapeutic massages or manual manipulation, and most are only seen once a month unless they have an acute flair-up of pain. Most inpatients offered therapeutic massage are those who are on palliative care service. At most, these patients receive a massage two or three times a week (**Figure 2**). Two palliative care patients wished for daily massages: "As they pass the meds out, pass me a massage." But as one participant observed, "Without somebody listening in Congress or the VA you're not gonna get another [therapist]."

A second issue involved the fact that many Veterans live ≥1 h driving time away from the VA medical center

- "I would do anything to meet the obligation to release pain. If it was required and available I'd be here more often."
- "It's obvious, she doesn't have time to get to everybody as quick as she'd like."
- "I haven't seen her in a while."
- "It's beautiful; they should have it for all Veterans."
- "It's not available to enough Veterans . . . and I don't get to be seen as much as I'd like to be seen."
- "Sometimes she's overwhelmed and I don't get the benefits even on a month to month basis."
- "If you only get one massage every 3 months, that's not effective at all."
- "I would like to see them be able to fund more massage therapists and more manual medicine people because your body is connected from the tip of your toes to the top of your head and if one place is irritated then it's going to affect the rest of your body and it also affects your temperament."
- "If I had my druthers, I'd be up here about every week."

Figure 2.
Patient quotes related to access to complementary and integrative health.

(an issue frequently found at other VA medical centers as well). "I'm 4 hours away." "I drive 80 miles [one way] to have this done and if it wasn't worthwhile I sure wouldn't make the trip." In response, the VA offers "fee-based" visits that allow Veterans to receive therapy in the local community provided by a non-VA provider. Although this sounds like a viable, if temporary, solution, participants cited problems here, too:

> I would have liked to have had more, but I guess it was a long, drawn out process, and I don't know why it stopped. I went and I filled out all the paperwork and it stopped, and I had to fill out paperwork again. He said it only goes for so long, and I was hoping to get some more extensive, but I don't know if I can do it here or it's more feasible for them to do it outside.

When asked about the paperwork involved to see a fee-based acupuncturist, a participant described it as, "Very, very complicated. There's a lot of paperwork and just running around." The participant eventually received acupuncture for a year, but then his primary care provider had to reauthorize further treatment.

Cost was a third issue affecting access. Because therapies such as yoga, Tai Chi, and acupuncture are not offered at the VA in which this study was conducted, participants reported having to use these therapies on their own. Referring to outside classes in Qigong and Tai Chi, a participant stated he did so only when he could afford it. A second stated he received CIH at the VA that day because a fee-basis authorization for acupuncture he received last year was not found. Another participant with PTSD who works with other Veterans with PTSD reported he has advised them to get massages, but, "Some of them were quite irritated that it was either not available or having to go to an outside source. Some of them were actually paying out of their own pockets because VA's not covering [the massage]."

Veteran-Specific Challenges

Service-connected conditions or situations were part of participants' conversations, whether discussing CIH or not. Participants associated being in the service as a specific cause of their pain and need for CIH but also described the "aftereffects of being in the service" on their lives in general. One long-term massage recipient described guarding large drums on piers without knowing the contents. He was now questioning whether they contained chemicals such as Agent Orange. Another described being exposed to extremely loud noises without adequate hearing protection. He concluded, "I'm very suspicious and not very trusting because of that. . . . It takes a long time for somebody to ever become really close to me. . . . My wife's put up with an awful lot of [expletive]." Their ongoing relationship with and trust in the therapist appeared to allow them to express these concerns.

Knowledge: Opioids and Complementary and Integrative Health

Even though 60 percent of the outpatients were currently taking opioids for pain relief (**Table 1**), they were particularly aware of problems associated with opioid use. One participant stated he was able to reduce his use of the pain medication Vicodin (hydrocodone/acetaminophen) due to receiving massage. Another participant cautioned against getting "hooked" on opioids. A third observed that pain medications do effectively control pain, "but

they make you feel worse in the long run." Yet another opined that having another therapy to offer Veterans before giving an addictive drug was "a tremendous idea." A fellow participant agreed that using massage instead of medication would be a lot better for PTSD or other types of depression and stress. The high cost of medications was the focus of another participant: "It's not good to have to take all of these drugs all the time and then have to keep track of them and get them reordered. It costs the government a lot of money. You might be able to eliminate a lot of that," implying CIH should be used more. Only one participant, an inpatient, made light of his drug use, stating he was eager to return home to an unlimited (illegal) supply of his drugs of choice.

Opinions

Complementary and Integrative Health Therapist

Praise for the massage therapist was overwhelmingly positive. While both inpatients and outpatients appreciated the massage itself, the outpatients particularly appreciated the additional lifestyle coaching and encouragement that the therapist provided. It was evident that the therapist's approach played an important part in the therapy.

Importance of Veteran Education and Relationships in Promoting Complementary and Integrative Health

One participant expressed a need for Veterans to be educated about massage. He illustrated his recommendations by describing Veterans as being "bad about relaxing" and considering massage as a waste of time "like a pedicure." Others emphasized the importance of the bond between Veterans when asked whether Veterans would accept CIH therapies. A participant thought that if a Veteran was approached by another Veteran who had experienced the CIH therapy, he or she would be much more accepting of CIH. Another stated that Veterans are "bad" about the thought of someone touching them, so they need to be educated about massage. When describing the chance for Veterans to talk with other Veterans during a VA wellness group, a participant opined that Veterans need to talk with someone "who has walked in their shoes" as opposed to a clinician who has "just read about it." Another said, "I can deal with it on a totally different level and that's important to a Veteran who has been through the wringer." A participant described CIH therapies that are promoted in the group as "very appealing" to Veterans. Another participant thought that CIH therapies "would probably be the best medicine" for PTSD, while another stated 4 out of 12 Veterans in his PTSD group were using CIH therapies. When describing how fellow Veterans had helped to calm a young Veteran who was crying in pain, a participant stated, "GIs have an interesting bond on each other, a lot of trust, a lot of respect, a lot of understanding."

Recommended Complementary and Integrative Health Therapies for Veterans

When asked to name the CIH therapies participants thought would appeal most to Veterans, inpatients chose massage, chiropractic, and music therapy while outpatients listed massage, yoga, acupuncture, and chiropractic therapy (**Tables 2–3**). Participants had not necessarily experienced a CIH therapy before recommending it. For instance, none of the inpatients had previously tried Reiki, aromatherapy, Qigong, touch therapy, or biofeedback, but one person recommended that each of those therapies be used in the VA. Two of the inpatients did not

Table 2.
Outpatient experiences with and recommendations for complementary and integrative health (CIH) therapies for Veterans (n = 15).

CIH Therapy	Used	Recommended
Massage[*]	15	13
Manual Manipulation[*†]	10	4
Diet/Herbal	9	2
Pet Therapy[*]	9	2
Meditation	8	—
Chiropractic	8	6
Aroma[*]	7	—
Transcutaneous Electrical Nerve Stimulation Unit[*‡]	7	1
Acupuncture	6	7
Music[*]	6	—
Biofeedback	6	5
Yoga	4	8
Qigong	3	—
Hypnosis	2	3
Touch	2	—
Tai Chi	2	1
Reiki	1	1
Mantram Repetition	1	—

[*]Offered at study Department of Veterans Affairs medical center.
[†]Osteopathic manipulative treatment for musculoskeletal pain and disability.
[‡]Therapeutic device used to stimulate nerves. It sends electrical pulses to surface of skin via electrodes that stimulate nerves.

Table 3.
Inpatient experiences with and recommendations for complementary and integrative health (CIH) therapies for Veterans (n = 15).

CIH Therapy	Used	Recommended
Massage*	14	10
Meditation	6	1
Chiropractic	5	5
Pet Therapy*	5	4
Music*	3	5
Yoga	2	4
Hypnosis	2	3
Diet/Herbal	2	3
Aroma*	2	1
Marijuana	2	—
Acupuncture	1	3
Water Aerobics	1	—
Reiki	—	1
Qigong	—	1
Touch Therapy	—	1
Biofeedback	—	1

*Offered at study Department of Veterans Affairs medical center.

feel comfortable recommending any of the CIH therapies. One stated that people from small towns like the one from which he came call people who use these types of therapies "Beverly Hillbillies," implying they try to act sophisticated when they are not.

Administrative Decisions

The participants were divided in their attitudes toward VA administration and the decisions that are made regarding funding priorities:

> The VA seems to be many, many times more interested in appearing to be concerned with Vets than they actually are being concerned about Vets. . . . Veterans don't care about the pictures on the wall. They don't care what color the floor tile is. . . . They seem to waste so much money on appearances that they could be actually putting toward improving treatment . . . the massage therapy, the manipulative medicine.

Another stated that servicemembers had been promised never to be left behind, but that due to the actions of people at both the local and national level, "There's a lot of Veterans that feel like they're left behind." A third stated, "The suits up on the ivory tower, they need to open their minds that there is a whole different universe outside of medical school and pharmaceutical industry pushing their programs."

However, not every participant agreed. One outpatient who spends a lot of time volunteering at the VA medical center stated that if there was something wrong he could always go to the local administration, which would listen to him and look into the complaint. Another observed, "I know they can't always satisfy me but I'll tell ya . . . I have no complaints. . . . They have to weigh the dollars. . . . We can't keep wasting." An inpatient also expressed concern that, as much as he enjoyed the massages, funding that was badly needed elsewhere should not be diverted solely for massages.

DISCUSSION

Because of their experiences in the armed forces, Veterans share both a distinctive bond and problems that are unique to them or magnified in prevalence compared with the general population. Chronic pain, estimated at 26 percent in the general population and over 44 percent in Veterans after combat, and illicit prescription opioid use, estimated at 4 percent in the general population and 15 percent after combat deployment, are excellent examples [22]. Hence, it is not surprising that pain was the common experience in this group of Veterans, whether related to a cancer diagnosis or other ailment. However, it is noteworthy especially for the outpatients that 60 percent of outpatients and 80 percent of inpatients were currently using opioids while at the same time recognizing the dangers inherent in continued opioid use. Acknowledging the problem of inappropriate opioid use, the VA recently issued a mandate to reduce the prescription of opioids [23]. The issue for Veterans is that the reduction of opioids without a satisfactory alternative to pain control potentially leaves the Veteran captive to chronic, often debilitating, pain as illustrated by the responses of the study participants, hence the overwhelming need for a nonpharmacologic alternative such as massage to be available on a consistent basis.

It is noteworthy that therapeutic massage appears to control pain severity by its effects on both physical and psychological symptoms, thus contributing to improved physical and mental well-being [13,24–25]. As illustrated by the participants' overwhelmingly positive responses, not only did they experience relief from physical pain through massage but they also related to the therapist on a personal basis. It was apparent that, in this situation, the physical manipulation of massage was only a part of the

therapy offered by the therapist in addition to teaching, coaching, encouragement, and therapeutic listening. Due to long-term contact with many of the participants, the therapist knew and understood them well. Thus, she was able to offer a much broader level of care than might be generally expected. The therapeutic interaction between the massage therapist and the patient transcended the pharmacological effect of opioids binding to receptors.

The type of care offered by the massage therapist is a perfect illustration of the VA's vision of offering personalized, proactive, patient-centered care. Although stated very differently, both VA administrators and the Veteran participants perceive an unfortunate negative influence of the medical model of care due to its emphasis on diagnosis and treatment as prescribed by the clinician, which may be slowing the acceptance of CIH therapies with their emphasis on what the patient considers important. They also agree that access is an issue, although they see the problem from different perspectives. While VA administrators describe the situation in administrative terms, including lack of position descriptions, inability to capture workload, misunderstanding about benefits, and the need for more evidence to back the use of CIH [20], the Veterans detail the issues immediately apparent to them, including the scarcity of providers, distances they have to travel to receive CIH therapies, and cost of care at least partly due to administrative snarls involving paperwork. However, while the perspectives differ from administrator to Veteran, basically they all agree that while increased access to CIH therapies, particularly massage, meditation, yoga, and acupuncture, is a priority goal, there are major issues of access plus provider and patient knowledge and opinions the VA must address in order to accomplish this goal.

Of note, to better address the problem of access, the VA has recently introduced the concept of Choice Cards, an option designed to allow Veterans to seek care outside of the VA if they cannot receive care within the VA in a timely manner. Beginning November 17, 2014, the VA began mailing the cards to Veterans waiting more than 30 d for an appointment at a VA facility. The VA then added an option that Veterans living more than 40 mi from a VA facility could also seek outside care. Whether these options will eliminate the problems for access to CIH described by the study participants remains to be seen.

A perhaps unexpected thread that came out of the participants' comments was the awareness of cost issues. While some criticized the VA for spending money on facilities rather than care, others expressed awareness that the VA needs to meet many priorities when making funding decisions. Several were also altruistic when considering their fellow Veterans, expressing concern that as beneficial as CIH is, money may be needed even more to provide basic medical care. The participants demonstrated awareness of the needs of other Veterans as well as themselves, reflecting the "no Veteran left behind" motto that is inculcated into servicemembers.

Interpretation of the findings of this study is limited by basing it on a convenience sample of Veterans receiving care from one massage therapist at only one VA facility. Although the Veterans were both inpatients and outpatients with a variety of diagnoses, they were primarily being treated due to chronic pain or the need for palliative care. A broader subject pool, e.g., users in pain due to other diagnoses, would have enhanced the findings and could be the subject of future research endeavors. Because subjects were already receiving one type of CIH therapy (therapeutic massage), their experience may have influenced the views they expressed regarding massage and/or other CIH therapies. However, the findings from the current study mesh with our previous study involving providers and administrators at the local level [20].

CONCLUSIONS

CIH therapies such as therapeutic massage offer a complementary form of therapy and/or rehabilitation that can reduce or sometimes eliminate opioid use for chronic pain. Although the promotion of CIH is important to the VA, the willingness of Veterans to use these therapies or the barriers to their use by otherwise willing Veterans need more attention. Furthermore, the willingness of Congress to fund such therapies in a contentious political climate is an important variable. As the VA goes forward with plans to reduce opioid use while promoting personalized, proactive, patient-centered care, e.g., through the use of CIH, it is essential to continue listening to what Veterans consider to be important goals as well as the obstacles to reaching those goals. It will also be important to evaluate the extent to which CIH therapies can improve clinical outcomes and result in cost savings to the VA and to educate and cultivate champions for their use in Congress.

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Initial development of a patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy

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Abstract—Guidelines on long-term opioid therapy recommend frequent reassessment of harm, efficacy, and misuse of these potentially harmful and sometimes ineffective medications. In primary care, there is a need for a brief, patient-reported instrument. This report details the initial steps in the development of such an instrument. An interdisciplinary team of clinician-scientists performed four discrete steps in this study: (1) conceptualization of the purpose and function of the instrument, (2) assembly of an item pool, (3) expert rating on which items were most important to include in the instrument, and (4) modification of expert-selected items based on a reading level check and cognitive interviews with patients. A diverse panel of 47 subject matter experts was presented with 69 items to rate on a 1–9 scale in terms of importance for inclusion in the instrument. The panel highly rated 37 items: 8 related to harm, 4 related to efficacy, and 25 related to misuse. These 37 items were then tested for patient comprehension and modified as needed. Next steps in development will include further item reduction, testing against a gold standard, and assessment of the instrument's effect on clinical outcomes.

Key words: chronic pain, efficacy, harm, instrument development, misuse, opioid analgesics, opioid therapy, pain management, patient reported, therapeutic monitoring.

INTRODUCTION

Patients and providers face complex challenges when managing long-term opioid analgesic therapy for chronic pain. Only a minority of patients may experience benefits from long-term opioid therapy [1–2], and this likelihood must be balanced against potential undesired outcomes, including safety issues ranging from mild toxicities to overdose and death [3] and misuse of these potent medications. To help patients and providers optimize outcomes and mitigate risks, experts advise a strategy of frequent reassessment of harm, efficacy, and misuse in patients on opioids to inform treatment decisions [4–5]. Assessment of harm, efficacy, and misuse of ongoing opioid therapy can be achieved through patient report, e.g., querying patients about side effects and therapeutic effects, and other methods, such as performing urine drug testing to assess for use of unprescribed substances [6] or querying a prescription monitoring database for evidence of multiple prescribers [7]. While the latter strategies are generally recommended and may be useful in the categories of harm and misuse, systematic assessment of patient-reported symptoms, emphasizing those that matter to

Abbreviations: IMMPACT = Initiative on Methods, Measurement and Pain Assessment in Clinical Trials; PRIOR = Patient-Reported Indications for Opioid Reassessment; VA = Department of Veterans Affairs; VHA = Veterans Health Administration.

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patients, has been recognized as a critical and often overlooked piece of high-quality medication management in general [8–9] and of ongoing opioid therapy in particular [4,10].

Experts have identified the phenomenon of clinical inertia—not making a change in therapy that may be indicated—as one of the factors driving the ongoing unprecedented rates of opioid prescribing [11–12]. Furthermore, there are emerging qualitative data from patients and providers about a troubling disconnect: the patient continues the therapy because the prescriber continues writing the prescriptions (not because the medication is effective) and the prescriber continues to write the prescriptions because of the untested assumption that the patient is satisfied with the treatment [13–14]. These findings drive our hypothesis that a brief instrument, protocolized into routine follow-up, may promote a more active surveillance approach and combat clinical inertia.

However, to date, there is no widely accepted, validated, patient-reported instrument available to monitor the harm, efficacy, and misuse of opioid therapy prescribed for patients with chronic pain. A recent systematic review identified nine published instruments that assessed at least one of these categories, none of which had been tested in clinical practice [15]. This shortcoming contributed to the conclusion that none of these instruments were comprehensive and feasible to implement in clinical practice. In light of this identified gap, our long-term goal is to develop such an instrument. The purpose of the present study was to describe the methods used to develop the preliminary version of an instrument designed to measure patient-reported harm, efficacy, and misuse of opioid therapy that will ultimately undergo further testing.

METHODS

Overview of Study Design

We performed four discrete steps in this study: (1) conceptualization of the purpose and function of the instrument, (2) assembly of an item pool, (3) expert rating of items from the pool most important to include in the preliminary version, and (4) modification of expert-selected items based on a reading level check and cognitive interviews with patients. Each component of the study was approved by the Department of Veterans Affairs (VA) Connecticut Healthcare System Human Subjects Subcommittee and the Yale University School of Medicine's Institutional Review Board.

Purpose and Function of Instrument

We convened a core research team, composed of clinician researchers with diverse training and experience in primary care/internal medicine, rheumatology, psychology, pain medicine, addiction medicine, nursing, psychometrics, and clinical epidemiology, to discuss the identified gap in opioid monitoring and establish the purpose and function of a new instrument. Consensus emerged that the instrument should be (1) developed for use in primary care, where most long-term opioid therapy is prescribed; (2) patient-reported and patient self-administered in order to improve efficiency and eliminate barriers to completion; (3) designed to be sensitive to incipient or developing harms and low or absent benefit; (4) complementary to existing measures of pain and opioid misuse; and (5) designed such that one or more positive responses to items on the instrument would prompt a more detailed clinical assessment of each positive response. As such, there would be no scaling or scoring of the instrument. We plan to name the final instrument the Patient-Reported Indications for Opioid Reassessment (PRIOR).

Assembly of Item Pool

We first performed a systematic review to identify instruments containing patient self-reported items related to safety, efficacy, and misuse of opioid therapy [15] and sorted items from these instruments (n = 9) by category (safety, efficacy, misuse, or other). The core research team reached consensus on whether this pool lacked any important items by comparing the list of efficacy-related items to the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT) recommended domains for assessing analgesic efficacy in clinical trials [16] and comparing the list of harm-related items with a literature search of opioid-related harms. Beyond these two sources, a suitable item was identified from the broader medical literature for any specific content area identified as missing.

Eliminating Items

First, we removed items that did not directly pertain to harm, efficacy, or misuse of current opioid therapy. Next, we identified items with identical or near-identical syntax and removed those items judged to have less clear syntax. We then removed items that were not written in patient-reported format if the item's content was covered

by a similar, patient-reported item. Since interpreting the clinical significance of single time point numeric ratings can be challenging [17], we removed items relying on numeric scales in the response if similar items not requiring use of a numeric rating scale were available. Finally, in recognition that three of the instruments identified in the systematic review were designed for clinical research on opioid-induced constipation (the Bowel Function Index, the Patient Assessment of Constipation Symptoms, and the Bowel Function Diary) and contained a level of detail on constipation unnecessary for primary care-based screening, we chose three items that adequately covered the concept of opioid-induced constipation rather than including all the constipation-related items.

Item Modification and Standardization

If a single item contained more than one content area, we revised it to create multiple items covering each one. For items not written in patient-reported format and if the content was not otherwise covered in one of the remaining items, we modified them into patient-reported format based on examples from the broader medical literature. To promote ease of evaluation by the expert panel and, ultimately, use of the instrument in clinical practice, we standardized the items in three ways. First, we edited each item to include a common stem, "In the last 30 days . . ." to fit the planned use of the instrument multiple times per year. With our goal of developing an instrument sensitive to harm-related problems, asking a patient to evaluate a symptom and additionally whether that symptom was related to or caused by opioids seemed unnecessarily complex and a potential source of low sensitivity. Therefore, when possible, we removed attribution of symptoms to opioids from items when such attribution was asked of the patient. If attribution was the crux of the question (e.g., "Have you been bothered by side effects of opioid pain medications?," we did not modify the item. Last, we transformed each item into a question with a yes/no response, whereby the "yes" response would denote an issue of clinical significance requiring more detailed assessment.

Subject Matter Expert Item Rating

A priori, we defined a subject matter expert as someone who (1) believes that, at least in some instances, opioids can be safely and effectively used for the treatment of chronic noncancer pain; (2) prescribes and manages opioids for chronic noncancer pain; and (3) has an established clinical or research interest in chronic pain management. We used two sources to identify potential subject matter experts: (1) the Veterans Health Administration (VHA) pain points of contact list, consisting of pain-interested clinicians responsible for dissemination and implementation of VHA pain-related policies at each VHA facility nationally (n = 108), and (2) the VHA pain research working group listserv, whose membership consists of VHA pain-relevant investigators (n = 30).

As is increasingly common, our expert item-rating process used an Internet-based survey platform (Qualtrics; Provo, Utah). We sent an email message to potential participants in which we provided a description of the project, noted the voluntary nature of participation, and embedded a link to the Web-based survey. In the survey, there were two screening questions regarding opioid therapy for chronic noncancer pain and a short demographics section. After describing the purpose of the instrument, we presented the participants with 69 items, sorted by category (harm, efficacy, or misuse), and asked them to rate each item on a 1–9 scale with respect to its importance for inclusion in the instrument (1 = not important, 9 = very important), based on the stated purpose of the instrument. Participants were asked to write in any items not listed that they believed should be included. Adapted from a published methodology [18], we identified the highly rated items using prespecified criteria: median response value of 8 or 9 with agreement, defined as 70 percent of values of 7, 8, or 9. We stipulated a priori that at least two items from each category would need to be present in the preliminary version of the instrument, even if they did not meet the definition of highly rated. We planned for the option of a second round of rating if there were new items suggested by subject matter experts or the absence of agreement on highly rated items.

Reading Level Check and Cognitive Interviews with Patients

An important step in the development of a patient-reported instrument, especially one that will be self-administered, is verifying that patients understand what the items mean [19]. To improve the comprehensibility of the items, we undertook two additional steps with the highly rated items: assessing the reading level of the items and performing cognitive interviews with patients on opioids. The reading level of each item was assessed using the Fog Index [20], which uses a scoring system of

reading level based on the numbers of words per sentence and the number of polysyllabic words per paragraph. Next, we performed cognitive interviews with patients in which, in 1:1 sessions, each patient was asked to read each item out loud and interpret, in his or her own words, what each item was asking. This "think aloud" procedure has been used in developing other patient-reported instruments [21]. Modifications were made for any item for which there was recurrent confusion. We conducted interviews until the most recent version was accurately interpreted by 10 consecutive participants.

RESULTS

Assembly of Item Pool

The **Figure** displays how the 129 items identified in the systematic review were reduced to the 69 items presented to the expert panel. Based on comparison to the domains recommended by IMMPACT, no items identified in the systematic review covered the specific efficacy-related content areas "functional interference" and "emotional interference." Therefore, we added one item each from the National Institutes of Health's Patient-Reported Outcomes Information System item bank related to these specific content areas [22]. Our literature review of opioid-related harms revealed two adverse outcomes—falls [23] and motor vehicle accidents [24]—not accounted for in the item pool; thus, we added an item about each [25–26].

Eliminating Items

The largest group of eliminated items were not written in patient-reported format but contained content covered elsewhere (n = 24). As mentioned previously, for parsimony while at the same time attempting to cover this common side effect, we retained three items related to constipation: "Have you been bothered by constipation?," "Have you been bothered by hard stools?," and "Have you been bothered by straining or squeezing to try to pass bowel movements?," and removed the rest (n = 20). The next largest group of eliminated items (n = 14) was judged as not directly pertaining to harm, efficacy, and misuse of current opioid therapy. Several of these items were historical in nature, e.g., "Have you ever had a drug or alcohol addiction problem?," and thus not practical for recurring use. Others sought to measure characteristics not directly related to the patient's own experience of harm, efficacy, or misuse, for example, "Do any of your family members disagree with your use of pain medications?" We eliminated 13 items with identical or nearly identical syntax to another item that was retained. For example, we considered "Is anyone in your family or among your friends concerned that you might be addicted to pain medications?" and "Family or friends have thought that I may be dependent on or addicted to opiate pain medications" nearly identical and eliminated the latter due to ambiguity of the term "dependent on." Four items relying on numeric scales, e.g., "What percentage of your pain has been relieved during the past week?," were eliminated.

Item Modification and Standardization

We divided items containing more than one component into single component items: for example, "I have felt depressed, down, or anxious" became "I have felt depressed," "I have felt down," and "I have felt anxious." We replaced non–patient-reported items not covered elsewhere with patient-reported versions. For example, the item "Ask patient about vomiting" was replaced by, "Have you been bothered by vomiting?," gleaned from a patient-reported instrument for gastric dysmotility [27]. Finally, to create binary items where a positive response was clinically meaningful, we inserted "bothered by" to reduce the possibility that the patient would endorse the item based on a clinically trivial level of symptoms, for example, "In the past 30 days, have you been bothered by constipation?" replaced, "In the past 30 days, have you been constipated?"

Subject Matter Expert Item Rating

The response rate to the survey for potential subject matter experts was 54 percent (75/138). Of the 75 respondents, 29 did not meet subject matter expert criteria (2 did not believe that opioids could be safely and effectively used in the treatment of chronic noncancer pain and 27 did not prescribe and manage opioid therapy for chronic noncancer pain). Of the 47 subject matter experts, 23 were women (49%), half were in the 46 to 55 yr age group, and each of VHA's 21 geographically contiguous catchment areas was represented. The largest group of subject matter experts was trained in general internal medicine/family medicine/primary care (n = 19), followed by pain/anesthesiology (n = 15), with addiction medicine, neurology, nursing, physiatry/physical medicine and rehabilitation, psychiatry, and rheumatology also represented. The expert panel highly rated 37 of the 69 items based on the criteria described; see **Appendix 1** (available online only) for complete results of the item

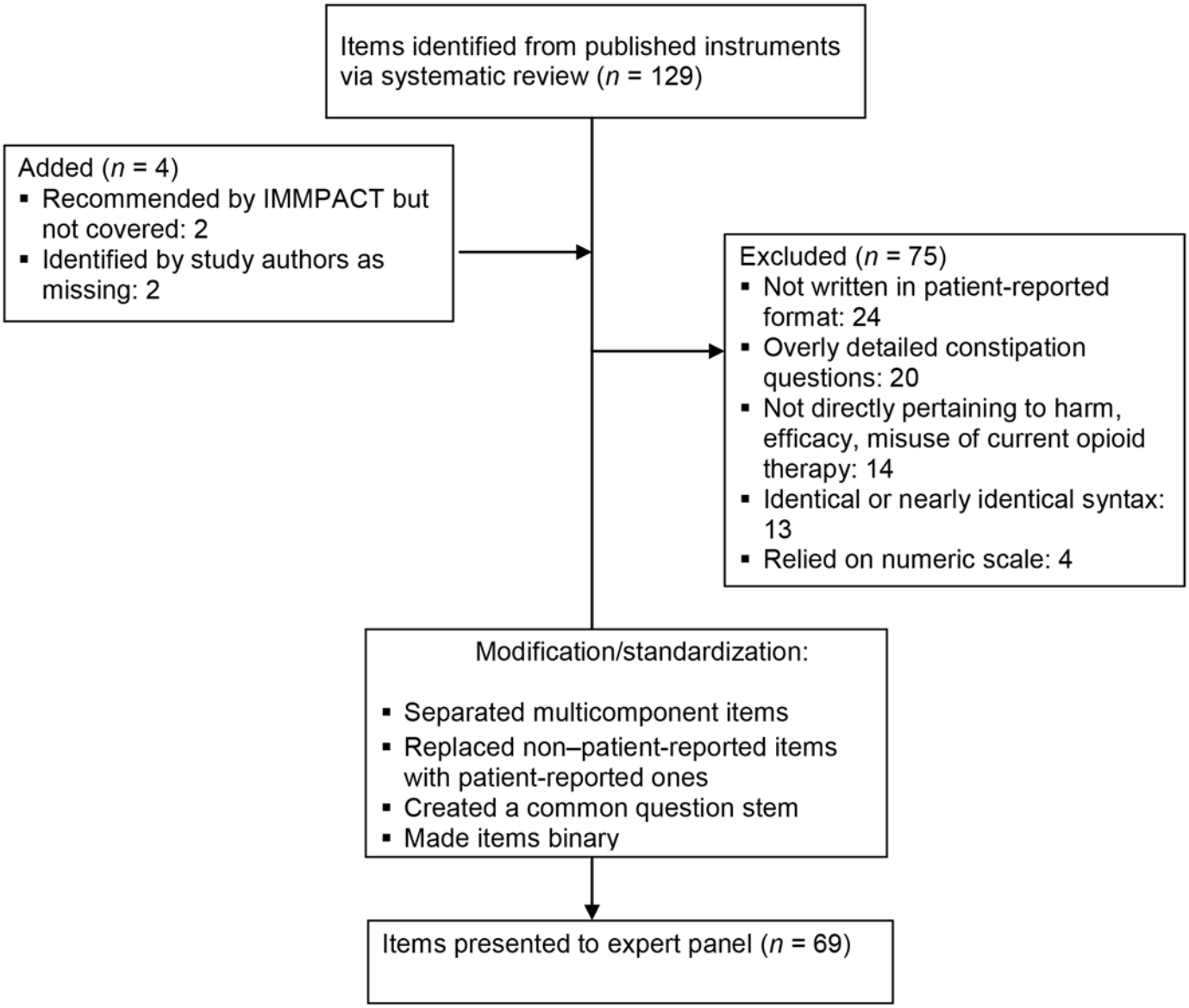

Figure.
Item pool development. IMMPACT = Initiative on Methods, Measurement and Pain Assessment in Clinical Trials.

rating process. Of the 37 highly rated items, 8 were related to harm, 4 were related to efficacy, and 25 were related to misuse. The median response value of each included harm-related item was 8, except "Have you felt sleepy or less alert when driving or operating machinery?," which had a median response value of 9. Since there was consensus on highly rated items and there were no new patient-reported items suggested by the expert panel, a second round of rating was not necessary.

In anticipation of further testing of the PRIOR in future studies, we consulted with the lead authors of the original instruments for permission to use their items. All but two authors granted permission, which affected two of the 37 items. For both items, we selected the next highest-rated item that was similar in content.

Reading Level Check and Cognitive Interviews

The reading level check did not lead to any item modifications because we had already shortened long

items in a previous step by breaking down multicomponent single items into multiple single-component items. Additionally, there was a low density of polysyllabic words. There was, however, heterogeneity among the items in how opioids were referred to and also whether the term "physician" or "doctor" was used. Based on the cognitive interviewing process, we identified "opioid pain medication" and "doctor" as the universally understood versions of these terms. Additionally, in the cognitive interviewing process, we learned that several patients thought the word "sedated" meant "knocked out" or "unconscious"; therefore, we changed this term to "overly drowsy" in keeping with other studies of centrally acting, sedating medications [28]. Following our a priori established protocol, the cognitive interviewing process was complete when 10 consecutive subjects interpreted all the items in the same way without confusion, which occurred after 16 interviews. The preliminary version of the PRIOR is contained in **Appendix 2** (available online only).

DISCUSSION

Through a multistep process, we developed a preliminary version of the PRIOR, a patient-reported instrument for identifying opioid harm, low efficacy, and misuse among patients on long-term opioids. The PRIOR is designed to fill a gap based on systematic review of the literature; accordingly, we aimed for it to be comprehensive, covering harm, efficacy, and misuse; to be patient-reported and patient self-administered in order to improve efficiency and eliminate barriers to completion, especially in primary care; and to yield clinically actionable information. Consistent with our goal of comprehensiveness, the subject matter expert panel in the present study highly rated at least four items from each of the harm, efficacy, and misuse categories. This spread of items across categories, while to some degree enforced by design, reflects the expert panel's interest in not just assessing traditionally provider-centered concerns (i.e., misuse), but also patient-centered ones (e.g., harm and efficacy). Feasibility is yet to be established. However, at 37 items, especially the 25 items related to misuse, this preliminary instrument is too long and will require further item reduction to be used in busy primary care practices. While several design decisions should promote the clinical utility of the PRIOR, this will ultimately be determined by field testing of a briefer version in subsequent studies.

The strengths of this work include, first, the rigorous approach to understanding the current needs in opioid monitoring through systematic review and also gathering input from a diverse research team with broad expertise. Second, the process for item selection brought together a large, diverse group of subject matter experts who efficiently arrived at consensus. Finally, the standardization of items and use of cognitive interviewing to ensure patient comprehension were critical steps often lacking in other instrument development processes.

A number of decisions in the design of the preliminary PRIOR deserve further discussion. The first is our decision to disaggregate previously validated multi-item instruments into their component items for voting by the expert panel. We considered this consistent with our overall conceptualization of the final PRIOR as a checklist of symptoms and behaviors in which each item would have its own inherent meaning and, if positive, would indicate the need for further clinical assessment. Additionally, the use of items from previously validated instruments afforded the advantage that each item had already been tested to some degree for patient comprehension or other validity. The next decision was to include only VHA clinicians in the expert panel. In recognition of the fact that VHA routinely uses other related instruments in clinical settings (e.g., the pain numerical rating scale, Patient Health Questionnaire-2 for depression), we are designing the PRIOR for use in VHA and thus wanted input from experts who work in the VHA system. Finally, we included nurse practitioners and physician assistants in the expert panel since these clinicians function as primary care providers in the VHA system and thus can contribute the same breadth of experience and expertise to this process.

The current study has limitations. First, while disaggregating other instruments may ultimately contribute to a brief, feasible instrument, it is possible that accuracy may be compromised if certain symptoms or behaviors are better assessed with intact groups of items. We consider this an acceptable trade-off of maximizing feasibility and sensitivity but sacrificing some specificity, which can be gained by the ensuing patient-provider discussion. Second, patient self-report of misuse may be inaccurate, especially when doing so may threaten future prescriptions [29], and yet over half of the preliminary PRIOR is misuse-related. We expect that in future development

steps, the number of misuse-related items will be reduced markedly; it may ultimately be determined that only one or two misuse-related items are worthwhile for use in a patient-reported instrument and that the bulk of the relevant data would come from non–patient-reported assessments such as urine drug tests, pill counts, and querying a prescription monitoring database.

CONCLUSIONS

As mentioned previously, next steps in this work include item reduction and field testing. To achieve that aim along with examining the psychometric properties of the instrument, we plan additional data collection and instrument analysis using Rasch methodology [30]. Patients taking opioids will self-administer the preliminary PRIOR as part of usual clinical care. Rasch analysis uses these data to create a hierarchy of the items on a unidimensional spectrum of difficulty, allowing elimination of misfitting and overcorrelated items and providing evidence for reliability and validity. Through this process, patient input will be incorporated since items that are never or very rarely endorsed will be dropped. The goal is to develop a briefer instrument with minimal respondent burden, which we will then compare against a standardized in-depth clinical assessment, including corollary non–patient-reported measures (e.g., urine drug testing and querying a prescription monitoring database), and finally test in clinical practice for its effect on harm, efficacy, and misuse-related outcomes. Our hypothesis is that the PRIOR will add significant value to the current standardized measures of pain intensity (e.g., the pain numerical rating scale) and opioid harm, but this hypothesis should be tested before broad dissemination. This preliminary version of the PRIOR provides a strong foundation for these future efforts.

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Stepped care model for pain management and quality of pain care in long-term opioid therapy

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Abstract—Successful organizational improvement processes depend on application of reliable metrics to establish targets and to monitor progress. This study examined the utility of the Pain Care Quality (PCQ) extraction tool in evaluating implementation of the Stepped Care Model for Pain Management at one Veterans Health Administration (VHA) healthcare system over 4 yr and in a non-VHA Federally qualified health center (FQHC) over 2 yr. Two hundred progress notes per year from VHA and 150 notes per year from FQHC primary care prescribers of long-term opioid therapy (>90 consecutive days) were randomly sampled. Each note was coded for the presence or absence of key dimensions of PCQ (i.e., pain assessment, treatment plans, pain reassessment/outcomes, patient education). General estimating equations controlling for provider and facility were used to examine changes in PCQ items over time. Improvements in the VHA were noted in pain reassessment and patient education, with trends in positive directions for all dimensions. Results suggest that the PCQ extraction tool is feasible and may be responsive to efforts to promote organizational improvements in pain care. Future research is indicated to improve the reliability of the PCQ extraction tool and enhance its usability.

Key words: chart extraction, chart review, chronic pain, organizational improvement, pain, pain care, pain management, primary care, quality indicators, Veterans.

INTRODUCTION

Chronic pain poses a substantial burden on the health of the U.S. population. Estimates suggest that over 100 million Americans experience persistent pain [1–2], with higher prevalence among Veterans [3] as well as medically underserved populations [4]. Among Veterans treated at Veterans Health Administration (VHA) primary care clinics, 50 percent report persistent pain [3,5]. A recent study in a large Federally qualified health center (FQHC) found that 40 percent of all adult ambulatory visits involved patients with chronic pain [6]. In addition, costs are estimated to exceed $600 billion in medical expenses and lost

Abbreviations: CHCI = Community Health Center Inc, EHR = electronic health record, FQHC = Federally qualified health center, PCP = primary care provider, PCQ = Pain Care Quality, SCM-PM = Stepped Care Model for Pain Management, VACHS = Department of Veterans Affairs Connecticut Healthcare System, VHA = Veterans Health Administration.

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productivity [7]. Although specialized multidisciplinary pain treatment is necessary and effective, particularly for more complex patients [8–9], access to these services is limited and is often not needed [7,10]. Thus, while most patients with chronic pain are treated by a primary care provider (PCP), most PCPs face organizational and administrative barriers to providing effective care [11], receive limited training in pain management [12–13], express low confidence in their ability to care for such patients [14–17], and hold reservations regarding treatment of chronic pain. Studies suggest that there is wide variability in PCPs' adherence to guidelines for pain management [18–20], and documentation of comprehensive pain care plans and specific treatment provided is poor [21–22].

Effective models of pain management in primary care have been developed. The most widely promoted evidence-based model is the Stepped Care Model for Pain Management (SCM-PM). The model, advocated by the American Academy of Pain Medicine [23], is the basis for the VHA's national pain management strategy [24–29]. It emphasizes an individualized, stepwise approach to pain management as patients increase in complexity and/or fail to achieve treatment goals with more conservative interventions [30]. Although several studies have demonstrated the potential for quality improvement initiatives to increase the quality of pain management, such initiatives are limited by a lack of well-established quality measures and benchmarks to measure their effect [6,22,30–32]. Recently, our group developed and validated a new tool for extracting information from electronic health records (EHRs) on the quality of documentation of pain and pain management [33]. Three dimensions of pain care quality were targeted, namely pain assessment (e.g., assessment of functioning and pain interference), treatment plans (e.g., patient education), and pain reassessment (i.e., assessment of outcomes). The current study was designed to further examine the psychometric properties of the measure with a specific focus on examining its responsivity to change in the context of a 5 yr performance improvement project designed to promote implementation of the SCM-PM with a specific focus on improved management of patients receiving long-term opioid therapy. Here we examine outcomes in one multisite VHA healthcare system, with replication and crossvalidation of the utility of this measurement approach in another multisite FQHC that was conducting a similar SCM-PM–based quality improvement initiative.

METHODS

Setting and Intervention

Department of Veterans Affairs Connecticut Healthcare System

The Department of Veterans Affairs Connecticut Healthcare System (VACHS) is composed of two academically affiliated VHA medical centers and six community-based outpatient clinics. About 50,000 Veterans receive care within VACHS annually. In addition to primary care services provided by an interdisciplinary team consistent with VHA's Patient Aligned Care Team model of care [34], VACHS PCPs and patients have access to a range of specialty pain management services, including rehabilitation, mental health, pain medicine, and complementary and integrative approaches.

Project Step was a 5 yr study designed to examine the adoption and implementation of SCM-PM throughout VACHS, with a particular emphasis on improvements to pain management in the primary care setting and appropriate referral to secondary specialty care [28]. From 2009 to 2012, a wide range of pain management-focused interventions were implemented, including policy and practice guidelines, templates in the EHR, increased access to complementary and alternative medicine providers, a rapid performance improvement workshop, a primary care pain workgroup, a PCP peer support group, and a wide range of PCP educational opportunities (a grand rounds series, Web access, round table meetings with pain specialty care, case-based interactive training, and workshops on improving patient communication).

Community Health Center Inc

Community Health Center Inc (CHCI) is a multisite FQHC located in Connecticut. CHCI provides comprehensive primary care services, including medical, behavioral, and dental care in 12 primary care health centers across the state as well as nearly 200 additional sites in schools and homeless shelters. CHCI cares for over 130,000 medically underserved patients in the state. Over 60 percent of CHCI patients are racial/ethnic minorities; over 90 percent are below 200 percent Federal poverty level, 60 percent are on Medicaid or state insurance, and 22 percent are uninsured.

Project STEP-ing Out was a 3 yr quality improvement initiative designed to improve pain care quality by applying the SCM-PM in a manner similar to Project

Step and evaluating the effectiveness of the model outside the VHA setting [6]. The project included implementation of a variety of organizational interventions that were introduced from 2010 to 2012. These included structured data collection and documentation tools, new standard policies for the management of chronic opioids, establishment of a chronic opioid "dashboard," annual pain-specific continuing medical education, integration of behavioral health pain management interventions, increased access to complementary and alternative medicine providers, and Project ECHO (virtual specialty consultation using video conferencing) [35].

Data Sources

All data for this study were extracted from primary care progress notes in the VACHS or CHCI EHRs. A random sample was selected of 200 patient progress notes for each of the four years for VACHS from July 2008 through June 2012 and 150 notes for each of the two years for CHCI from January 2011 through December 2012. Progress notes were eligible for patients enrolled for care at VACHS or CHCI who had received 90 consecutive days or more of prescription opioid medications for pain by a PCP within the study year. Patients prescribed opioids for cancer pain, for substance use disorder, for other nonpain uses, solely by a specialty-care or other nonprimary care provider, or outside of the specified setting (VACHS or CHCI) were not included. Notes were evaluated for any time during the entire study year rather than only during the period for which the patient was prescribed opioids. Within VACHS, the number of patients who received 90 consecutive days or more of opioid medications for pain was 552 for year 1, 596 for year 2, 578 for year 3, and 535 for year 4. Within CHCI, there were 1,058 patients who received ≥90 consecutive days of opioid medications for pain in 2011 and 1,308 in 2012.

Measures

Details of the development and characteristics of the chart abstraction tool have been previously published [33]. The tool contains 12 indicators grouped into three domains: pain assessment, pain treatment, and reassessment. Pain assessment targeted information gathered by the PCP to help with diagnosis and treatment, including assessment of the presence of pain, the source of pain, or the effect on patient functioning, and a review of any recent pain tests or diagnostics. Pain treatment included entering a consult for pain-related specialty services (e.g., chiropractic, pain medicine clinic, physical therapy), ordering a diagnostic test, prescribing a medication, documenting a specific plan for treatment, and/or providing education/information. Pain reassessment addressed whether PCPs checked in with patients about the effectiveness of current pain treatments and whether pain and/or functioning have changed since the previous visit. For each progress note, the rater read all available clinical notes and data fields for that date. The rater then coded whether each individual indicator was present or absent. A comprehensive coding manual was developed at each site detailing operational definitions for each domain and individual indicators, guidelines for coding specific frequently occurring content in PCP notes, and specific examples of cases that met or did not meet criteria for each indicator. Raters were trained by a physician or psychologist with extensive clinical experience with the specified EHR. Training included reading and reviewing the coding manual and addressing questions and discussing distinctions and variations, guided coding of example notes, and review of notes coded by both the trainer and the rater. For notes coded by both the trainer and rater, inconsistent codes were reviewed directly and resolved through consensus by consulting the coding manual or discussing with other members of the research team. Additional reliability checks were performed randomly after initial training to avoid drift. The prior study by our group found that the measures of interrater reliability ranged from $\kappa = 0.56$ to 1.00 [33].

Procedures

Each of the randomly selected progress notes was examined by a trained research assistant using the chart abstraction coding manual. Cases were excluded for the following reasons: (1) patients did not have a routine primary care visit with their PCP within the 1 yr time period; (2) the only primary care encounter was one in which the patient saw only the nurse and not the PCP; (3) the only primary care encounter was an unscheduled or urgent, rather than routine, visit and would thus not be focused on the presenting problem and not necessarily include assessment of pain; or (4) the only primary care encounter was an initial rather than follow-up visit with the PCP, for which many of the extraction items, such as reassessment of pain and review of assessments, would not be possible. For VACHS, there were a total of 689 included progress notes over the four years. For CHCI, there were 300 included progress notes.

Data Analysis

Analyses were conducted separately for each setting. Generalized estimating equations with logit link and autoregressive covariance matrices were used to estimate the proportion of charts coded for the presence of each Pain Care Quality (PCQ) extraction tool item for each year and type of facility (health center or community-based outpatient clinics in the VACHS and small [1–2 PCPs], medium [3–4 PCPs], or large [5 or more PCPs] clinics in the CHCI). Analyses controlled for PCP and the repeated measures within PCP in each of the years of observation. Planned follow-up contrasts evaluated the linear trend over the four years. All analyses were conducted using SPSS 19.0 (IBM Inc; Armonk, New York). Cohen kappa was used to evaluate interrater reliability in the VACHS.

RESULTS

Department of Veterans Affairs Connecticut Healthcare System

Table 1 presents measures of reliability and outcome estimates for each PCQ extraction outcome within the VACHS sample. The sample was predominately male (96.7%), and the mean age was 62.5 yr. Reliability measures (Cohen kappa) were based on 114 cases over the four years. Kappa indices ranged from 0.50 to 1.0 and were somewhat lower for the intervention outcomes (0.63–1.00 for assessment outcomes and 0.50–0.87 for intervention outcomes).

Controlling for provider and treatment location, there were significant changes over the four years for provider assessment of function, review of recent tests and diagnostics, ordering of pain-related consults, documentation of a specific treatment plan, pain education, and reassessment. Evaluating the linear trend over the four years, there were significant increases for documentation of review of recent tests and diagnostics ($p = 0.001$), pain medication prescriptions ($p = 0.03$), and reassessment ($p = 0.005$) and decreases for consult orders ($p = 0.02$) and specific pain treatment plan ($p = 0.001$). There was a marginally significant trend for increasing assessment of presence of pain ($p = 0.05$) and decreasing orders for diagnostics ($p = 0.06$). Documentation of pain education was higher in years 2 and 4 than years 1 and 3 ($p = 0.002$). Pain intensity ratings increased significantly over the four years ($p = 0.006$ for the linear trend).

There were significant differences in documentation by medical facility type, with higher rates of presence of pain ($p = 0.006$), patient function ($p = 0.02$), pain source ($p = 0.001$), review of tests and diagnostics ($p = 0.001$), specific pain treatment plan ($p = 0.001$), and reassessment ($p = 0.03$) in health centers than in the community-based outpatient clinics. There were no significant interactions of medical facility type and year.

Table 1.
Percent of patient charts with endorsed pain care quality outcomes in Department of Veterans Affairs Connecticut Healthcare System by year.

Measure	Kappa*	Project Step Year				*p*-Value
		2008–2009, *N* = 174	2009–2010, *N* = 175	2010–2011, *N* = 160	2011–2012, *N* = 180	
Pain Intensity Rating	—	4.4	5.1	5.2	5.41	0.04
Assessment	1.00	98.3	96.0	99.4	97.8	0.05
Presence	1.00	93.7	96.0	98.8	97.8	0.14
Function	0.63	38.5	42.3	23.8	48.9	<0.001
Source	0.87	96.0	94.3	95.0	97.2	0.54
Review	0.70	24.7	41.1	38.8	45.0	0.001
Intervention	0.82	98.9	96.0	98.8	99.4	0.15
Medication Ordered	0.51	96.6	94.3	98.8	98.9	0.06
Consultation Ordered	0.73	16.1	10.3	15.0	6.7	0.02
Specific Pain Plan	0.50	78.2	73.1	58.8	68.3	0.001
Pain Education	0.63	11.5	25.7	14.4	22.8	0.003
Diagnostic Ordered	0.87	8.6	9.1	4.4	5.0	0.18
Reassessment	0.65	53.5	72.0	59.4	73.9	<0.001

*Based on 114 notes double coded for reliability.

Community Health Center Inc

Table 2 presents measures of reliability and outcome estimates for each PCQ extraction outcome within the CHCI sample. The sample was predominately female (59.7%), and the average age was 49.5 yr. Kappa values at CHCI were not calculated due to limited resources and unavailability of additional raters. During the training process, a research assistant and a senior researcher who had previously worked at the VACHS with Project Step and contributed to the development of the PCQ tool reviewed sample patient progress notes separately and compared their findings until they reached 10 consecutive cases for which they had 100 percent consensus in coding.

Controlling for provider and treatment location, there were no significant changes over the two years of evaluation. There were significant differences in documentation by medical facility type. Large facilities had lower documentation of presence of pain ($p = 0.005$) compared with small and medium facilities. Small facilities had greater documentation of pain education compared with medium and large facilities ($p = 0.006$). There were no significant interactions of medical facility type and year.

DISCUSSION

The VHA has established an evidence- and population-based SCM-PM as its single standard of pain care [28–29]. Despite growing empirical support and enthusiasm for the SCM-PM, there currently exists no methodology for evaluating the degree to which this new standard has been implemented. To address this gap, we have defined the key dimensions of PCQ as pain assessment, treatment (including pain education), and reassessment [33]. Our definition is informed by VHA policy that established these key dimensions as standards of pain management, including standards for assessing outcomes and quality, and benchmarks for provider competencies and expertise. Our team has completed foundational work to develop reliable and valid metrics for assessing these key dimensions of PCQ using chart review to extract the data from the EHRs. Ratings of interrater agreement over the study period were consistent, ranging from 0.50 to 1.0, with two values indicating "fair," five indicating "good," and five indicating "excellent" reliability [36–37]. There was greater reliability for the overall domains of pain assessment and treatment planning and lower reliability for most of the individual items [38]. This study extends these findings in significant ways by providing further evidence of the reliability and responsivity to change of this measure in a VHA setting while replicating its usability in a non-VHA community-based integrated healthcare setting.

Table 2.
Percent of patient charts with endorsed pain care quality outcomes in Community Health Center Inc by year.

Measure	Year		*p*-Value
	2011, *N* = 150	2012, *N* = 150	
Pain Intensity Rating	6.0	6.3	0.40
Assessment	76.7	80.0	0.61
Presence	65.3	71.3	0.43
Function	6.7	10.7	0.24
Source	64.0	66.7	0.79
Review	4.7	8.7	0.18
Intervention	100.0	100.0	>0.99
Medication Ordered	100.0	100.0	>0.99
Consultation Ordered	10.0	10.7	0.87
Pain Plan	96.0	95.3	0.61
Pain Education	16.0	18.7	0.57
Diagnostic Ordered	21.0	27.0	0.22
Reassessment	20.0	28.7	0.09

At VACHS, a number of PCQ components were responsive to change over time and type of clinic. Findings showed evidence of improved PCP assessment of patient functioning, review of tests and diagnostics, pain education provision, medication prescription, and pain reassessment. These findings are consistent with Cleeland et al., who found improvement in provider pain management documentation over an 8 mo rapid improvement process across five primary care sites in VHA [30]. There was also evidence of a decline in ordering of pain specialty consultations (such as pain medicine, rehabilitation, and chiropractic). However, these findings contrast a recent evaluation of VACHS EHR data among recipients of opioid prescriptions for noncancer pain, which found increased referral and use of complementary and alternative treatments for pain, such as chiropractic and physical therapy [38]. It is possible that the chart extraction item is too broad and may be identifying trends across different types of referrals.

Although interrater agreement ranged from "fair" to "excellent," two items had only "moderate" or "fair" overall reliability (medication ordered, kappa = 0.51, and specific pain plan, kappa = 0.50) [36–37]. Medication

ordered may have been affected by the high overall prevalence of medication orders [39]. Of note, although the measure of reliability for medication orders was lower, the prevalence was consistently high across all years for VACHS (>94%) and 100 percent across both years within CHCI. This suggests that for patients on long-term opioids, this item may not be responsive to change over time, likely because medications (opioids or nonopioids) will continue to be prescribed for these patients. It may also be possible that coders had a difficult time distinguishing whether medications commonly used for pain management, such as antidepressants and anticonvulsants, were being prescribed for this indication or for a mental health or other comorbid condition. Similarly, for the specific pain treatment plan, the item was intended to capture documentation of plans of any prescribed activities for treating pain, including medications. However, coders may have had difficulty distinguishing possible alternative treatment for pain that may have been presented. Operationally defining this item was difficult, and additional specification and training may be needed to improve reliability, or it may be more practical to separate the item into components that are more reliably coded. Thus, the lower reliability of these items may have affected the evaluation over time.

Although most of the results were consistent with improvement in PCP pain care management, some findings were equivocal. There was an increase in medication prescriptions for pain. Although our methods did not evaluate whether the increases were in opioid or nonopioid pain medications, it is noteworthy that the pool of patients receiving opioid medications over the 4 yr study period appears to have decreased, and our recent evaluation of VACHS EHR data [38] showed an overall increase in nonopioid prescriptions and decrease in high-dose opioids over the same time frame, indicative of overall improved pain care. One somewhat troubling finding was a decrease in documentation of a specific treatment plan for pain management. Given the increase in pain education and decrease in consultations, it is unclear whether this change represents less provider clarity in patient treatment or whether providers are exploring new treatment options that may require additional evaluation. Additional qualitative evaluation of providers' treatment processes would be informative.

Within the Federally qualified CHCI setting, the PCQ extraction tool was found to be usable and provided information on commonly documented components of pain care quality (assessment of pain presence and source, medication prescriptions, and specific pain treatment plans) and those with low documentation (assessment of function and review of tests and diagnostics and pain education, ordering of consultation and diagnostics, and reassessment). The findings noted in VACHS were not replicated in the 2 yr evaluation in this setting, although estimates were nominally in the expected direction, suggesting that the time period may have been insufficient to evaluate the effect of the wide array of interventions implemented.

Despite the fact that the study was not designed or powered to examine PCQ documentation by type of facility in both settings, we decided that such analyses might be informative. The fact that facility type did not interact with time suggests that improvements were similar in both settings. The pain management-focused interventions in both VACHS and CHCI were implemented across facility types, with a number of features designed to involve providers from all types of facilities. In VACHS, quality of documentation appeared to be better in larger health centers than in community-based outpatient clinics across the four years. In contrast, documentation was greater in smaller CHCI clinics than in larger ones. These findings suggest that performance improvement efforts may be enhanced by taking into account facility characteristics.

Several limitations of this study are important to acknowledge. First, the findings were based on opioid prescribing in primary care only, and thus patients prescribed opioids solely by a specialty care or other nonprimary care provider, or prescribed outside of VHA were not included. Based on other analyses on this topic, we believe that these are likely a small number of patients, but we do not know how much they differ from patients in the current study. Second, the findings are based on documentation within the EHR of pain management rather than observation of provider behavior. As has been noted by Krebs et al. [22], this likely represents an underestimate of provider pain activities. Thus, the interventions implemented in both settings may have affected provider reporting behavior without affecting underlying pain management behavior, or the reverse. Third, despite the large number of PCP encounters extracted and coded each year, there were indications of substantial variability in several of the measures. For example, in the VACHS setting for all measures that showed significant changes over time (functioning, review, planning, education,

consult ordered, and reassessment), there were numeric changes from year 2 to year 3 inconsistent with the overall trend over the four years. Increasing the number of encounters extracted and coded would improve measurement precision for evaluating changes within providers over time, as would controlling the number of encounters within PCP. Similarly, although ratings of interrater reliability were generally in the moderate to excellent range, measurement error may have limited power to evaluate the effect of the implemented interventions on provider pain management behavior, including the nonsignificant effects in CHCI.

Finally, responsivity of the measure to performance improvement efforts might be improved by assessing quality of pain care as continuous rather than multiple dichotomous measures. We considered an overall measure of PCQ as the sum of the individual components. However, it is unclear whether the components should be equally weighted to measure overall PCQ, whether improved PCQ is based on decreases in some components and increases in others, and whether some components may be better measured as continuous or ordinal measures rather than simply categorical. Further evaluation and development of measures that address component importance, direction, and degree are warranted.

CONCLUSIONS

Our study provides evidence of the potential utility of our PCQ extraction tool in the context of organizational efforts to promote implementation of an evidence-based SCM-PM specifically targeting improvements in management of patients receiving long-term opioid therapy for chronic pain. Overall, results suggest some improvements in the quality of pain care at two institutions over several years of investigation, although the magnitude of these changes is modest and inconsistent across setting and quality indicator. Although our results encourage the use of the PCQ extraction tool in similar efforts, there are several implications for further developments. First, raters found it challenging to code some subdomains reliably, and efforts are underway to refine the operational definitions and coding manual to improve interrater agreement. Second, the current version of the measure is limited by the binary (yes-no; present vs nonpresent) nature of the coding process. Future efforts to permit reliable coding of degrees or level of quality for each of the indicators would likely prove useful. Third, it similarly may be useful to examine a summary index of PCQ based on the individual domains of the measure. Finally, the current manual record review approach is extraordinarily time consuming and labor intensive. Development of an automated approach using machine learning and natural language processing promises to yield increased reliability and utility of the measure. Taken together, a more efficient, reliable tool with readily interpretable summary indices could likely improve the responsivity of the measure to change and encourage its use in similar pain-relevant organizational improvement efforts.

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Implementation of telementoring for pain management in Veterans Health Administration: Spatial analysis

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Abstract—In 2011, the Veterans Health Administration (VHA) implemented a pilot telementoring program across seven healthcare networks called the Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO) for pain management. A VHA healthcare network is a group of hospitals and clinics administratively linked in a geographic area. We created a series of county-level maps in one network displaying (1) the location of Veterans with chronic pain, (2) VHA sites (i.e., coordinating center, other medical centers, outpatient clinics), (3) proportion of Veterans being seen in-person at pain specialty clinics, and (4) proportion of Veterans with access to a primary care provider participating in Pain SCAN-ECHO. We calculated the geodesic distance from Veterans' homes to nearest VHA pain specialty care clinics. We used logistic regression to determine the association between distance and Pain SCAN-ECHO primary care provider participation. Mapping showed counties closer to the Pain SCAN-ECHO coordinating center had a higher rate of Veterans whose providers participated in Pain SCAN-ECHO than those further away. Regression models within networks revealed wide heterogeneity in the reach of Pain SCAN-ECHO to Veterans with low spatial access to pain care. Using geographic information systems can reveal the spatial reach of technology-based healthcare programs and inform future expansion.

Key words: chronic pain, distance, ECHO, geographic information system, GIS, healthcare access, spatial, telemedicine, telementoring, Veteran, Veterans Health Administration.

INTRODUCTION

Technology-based healthcare programs designed to train primary care providers in the management of complex chronic conditions are being increasingly implemented [1–2]. The Project for the Extension for Community Healthcare Outcomes (Project ECHO) is one such telementoring program that initially focused on hepatitis C and has since expanded to other specialties, including chronic pain [3]. Past evaluations of Project ECHO (and other telementoring) initiatives have focused on comparative effectiveness of technology-based healthcare [4], assessment of intermediate patient outcomes [5],

Abbreviations: CI = confidence interval, GIS = geographic information systems, NRS = numeric rating scale, OR = odds ratio, Project ECHO = Project for the Extension for Community Healthcare Outcomes, SCAN-ECHO = Specialty Care Access Network-Extension for Community Healthcare Outcomes, VA = Department of Veterans Affairs, VHA = Veterans Health Administration.

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descriptions of programmatic scope [6], and qualitative data from providers' perspectives on barriers and facilitators [7]. A major goal of these initiatives is to overcome barriers to accessing specialty care. Specifically, distance from the nearest specialty care provider has been shown to be a barrier in multiple studies. However, prior spatial evaluations of technology-based healthcare programs have been limited to summaries of miles saved and maps of participating clinics [8–9].

Up to 50 percent of Veterans have one or more chronic pain conditions [10]. Further, up to 36 percent of Veterans live in rural areas [11]. These rural Veterans face geographic barriers to pain specialty care as Veterans Health Administration (VHA) specialty pain care clinics are typically located in urban medical centers. Starting in 2011, the VHA began a program based on Project ECHO called the Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO). The SCAN-ECHO program included a focus on chronic pain and sought to improve chronic pain care by extending specialty care expertise to primary care providers caring for Veterans who live far away from medical centers with pain specialists. To our knowledge, previous studies have not examined the spatial penetration of a specialty-specific telementoring program, contextualized by the underlying location of the target patient population and spatial barriers to specialty care.

The objective of this study was to evaluate the spatial reach of the VHA's Pain SCAN-ECHO program, contextualized by the spatial distribution of Veterans with chronic pain and in-person specialty pain care in seven VHA healthcare networks. Specifically, within one sample healthcare network with a Pain SCAN-ECHO program, we used geographic information systems (GIS) to map (1) the location of Veterans with chronic pain, (2) VHA sites (i.e., coordinating center, other medical centers, outpatient clinics), (3) proportion of Veterans being seen in-person at pain specialty clinics, and (4) proportion of Veterans with access to a primary care provider participating in Pain SCAN-ECHO. Using distance from Veterans' homes to nearest pain specialty care as a marker of spatial access, we used logistic regression models at the patient level to describe the association between access to specialty pain care and SCAN-ECHO primary care provider participation. We used similar logistic regression models to describe the association between access to pain care and in-person utilization as a comparison. Consistent with the goals of the Pain SCAN-ECHO program, we hypothesized that greater distance from pain specialty care would be associated with increased primary care provider participation.

METHODS

Population and Setting

We identified all Veterans in seven VHA networks with chronic pain, defined as reporting at least one pain numeric rating score (NRS) ≥4 during any inpatient or outpatient encounter in at least 3 distinct calendar mo during any 12 mo period from April 1, 2010, to December 31, 2013 (n = 410,780) (**Figure 1**). This definition of chronic pain is consistent with prior literature [12]. During inpatient and outpatient encounters, VHA patients report current pain using the NRS, with 0 equivalent to no pain and 10 equivalent to the worst possible pain [13]. We identified all primary care encounters starting 60 d prior to the first reported pain intensity rating. Veterans were linked to a primary care provider if they had at least three visits with the same provider. All Veterans with chronic pain in this study were successfully linked to primary care providers. Patients linked to primary care providers outside of the seven networks were excluded (n = 22,323). We excluded patients whose home address was missing (n = 8,420). We used GIS to determine whether a Veteran's home address was within the spatial boundaries of one of the seven healthcare networks. We included border counties of these networks. We excluded Veterans whose home address was not within those boundaries (n = 8,391).

Pain SCAN-ECHO Program

In 2011, the VHA implemented the Pain SCAN-ECHO program in 7 out of the 21 VHA healthcare networks. The VHA SCAN-ECHO program has been previously described [6]. Briefly, the SCAN-ECHO program uses communication technology such as video-conferencing to facilitate case-based mentoring between specialty care providers at coordinating centers and primary care providers at remote clinics. SCAN-ECHO participation is voluntary, and participating primary care providers receive continuing medical education credit. Primary care providers who presented patient cases at at least one Pain SCAN-ECHO sessions were considered exposed to the Pain SCAN-ECHO program on the date of their first case presentation. Participation was validated by coordinating centers.

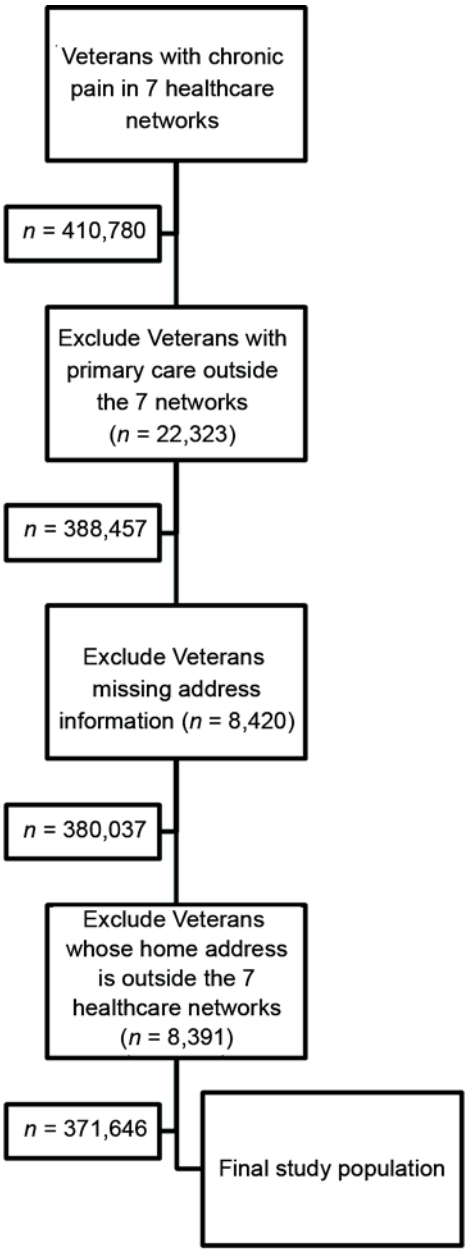

Figure 1.
Description of cohort exclusion criteria.

Patients were considered exposed to Pain SCAN-ECHO on the date that their primary care provider presented his or her first Pain SCAN-ECHO session.

Pain Clinic Identification

Specialty pain clinics are not available at every VHA medical center and clinic. We created a binary variable for whether pain specialty care was available at medical centers or clinics based on the observed number of nontelemedicine specialty pain clinic outpatient encounters of this chronic pain cohort. Specialty pain care is primarily available at medical centers. However, some community clinics offer specialty pain care. We contacted 15 sites with a borderline number of visits directly to assess specialty pain care availability, which informed our definition of specialty pain care availability. Medical centers with ≥100 nontelemedicine visits coded with a pain clinic stop code were considered specialty pain care sites. Outpatient clinics with ≥200 nontelemedicine visits coded with a pain clinic stop code were considered specialty pain care sites. Outpatient records, including site identifiers, were used to determine whether a Veteran had an in-person encounter in specialty pain clinic (i.e., not coded as telemedicine) in one of the sites with specialty pain care. Veterans meeting these criteria were considered to have received in-person specialty pain care.

Geographic Information Systems

Geographic files of the seven VHA networks and geocoded facility locations and designations were obtained from Department of Veterans Affairs (VA) Planning Systems and Support Group. United States' county, state, and nation boundaries were obtained from the U.S. Census Bureau. Veterans were aggregated to counties and health networks using GIS to determine whether a home address was within a county or health-network border. We calculated the geodesic ("as the crow flies") distance in miles from every Veteran's home to the nearest VHA facility designated a specialty pain care facility. This distance was used as a surrogate for access to pain care. We created a series of maps in a sample VHA network to display the geographic distribution of (1) the underlying distribution of Veterans with chronic pain, (2) the distribution of Veterans with access to a primary care provider participating in Pain SCAN ECHO, and (3) the distribution of Veterans seen in-person by specialty pain care.

Statistical Analyses

Each Veteran's rurality status was based on previously described classifications of urban, rural, and highly rural [14]. Highly rural Veterans were collapsed with rural Veterans to obtain a binary patient-level variable of urban or rural. Patient-level traits were aggregated to networks to establish the total number of Veterans with chronic pain, patients exposed to SCAN-ECHO, and patients who received in-person specialty pain care in each of the

seven networks. Within each network and overall, the distribution of the distance from Veterans' homes to the nearest specialty pain care site was summarized as a median and interquartile range. We also calculated the proportion of patients living within 50 miles of a specialty pain care site.

We used logistic regression to determine the association between (1) distance and pain specialty care and (2) distance and Pain SCAN-ECHO primary care provider participation. Both models were fit for the entire population and for each network individually and summarized as odds ratios (ORs) with 95 percent confidence intervals (CIs) based on profiled likelihoods. The goal of these models was to quantify and contrast the overall relationships between the outcomes (SCAN-ECHO provider participation and in-person pain care) and distance. Accordingly, these models were not adjusted for other covariates. Preliminary data cleaning was done using SAS, version 9.3 (SAS Institute Inc; Cary, North Carolina). All logistic regression, GIS analyses, and mapping were done with R, version 3.1 (R Foundation for Statistical Computing; Vienna, Austria).

RESULTS

Patient Characteristics

In the seven healthcare networks participating in the pilot Pain SCAN-ECHO program, we identified 371,646 patients with chronic pain using VA primary care who met study criteria (**Figure 1**). Among these patients, 6.7 percent (n = 25,168) were part of the patient panels of primary care providers who presented ≥1 case at Pain SCAN-ECHO sessions, and 17.3 percent (n = 64,394) had an in-person specialty pain care clinic visit. The median distance from a patients' home to the nearest pain specialty care clinic was 17.04 miles (interquartile range = 7.24–39.02). Overall, 81 percent of patients lived within 50 miles of a pain specialty clinic. The population was 22.5 percent rural (**Table 1**).

Healthcare Networks

There were seven healthcare networks with multiple U.S. states per network that contained a Pain SCAN-ECHO program. The distribution of patients' median distance to specialty pain care showed large network variation, with median distance ranging from 10.6 to 28.7 miles, and the proportion of patients living within 50 miles of pain specialty care ranging from 62 to 96 percent (**Table 1**). There was also significant network variation in both the proportion of chronic pain patients seen in a specialty pain care clinic (ranging from 10.5% to 21.5%) and the proportion cared for by a provider participating in Pain SCAN-ECHO (ranging 1.8% to 19.3%) (**Table 1**).

Spatial Distribution

Using GIS mapping in a single network as an example, the density of Veterans with chronic pain mirrored the general VHA population, with a higher number of

Table 1.
Characteristics of Veterans Health Administration (VHA) networks participating in Pain Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO).

VHA Healthcare Network	Total No. Veterans with Chronic Pain, *n*	Total No. SCAN-ECHO-Exposed Patients, *n* (%)	Total No. Veterans Seen at In-Person Pain Specialty Care, *n* (%)	Proportion of Veterans with Chronic Pain Living <50 miles from Pain Specialty Care	Distance from Veteran Home to Pain Specialty Care, Median (IQR) (miles)	Proportion of Veterans Classified as Rural
All	371,646	25,168 (6.7)	64,394 (17.3)	0.81	17.04 (7.24–39.02)	0.23
1	45,744	3,892 (8.5)	9,116 (19.9)	0.88	18.63 (8.94–33.48)	0.27
2	47,391	849 (1.8)	8,021 (16.9)	0.89	17.95 (6.67–33.55)	0.23
3	64,682	2,158 (3.3)	8,994 (13.9)	0.80	27.34 (10.42–46.55)	0.34
4	52,347	10,082 (19.3)	10,977 (21.0)	0.96	10.64 (4.82–22.73)	0.22
5	50,540	2,033 (4.0)	7,826 (15.5)	0.62	20.17 (7.57–91.61)	0.24
6	39,705	2,723 (6.9)	4,157 (10.5)	0.60	28.72 (6.50–142.57)	0.29
7	71,237	3,431 (4.8)	15,303 (21.5)	0.89	12.8 (7.92–24.36)	0.05

Table 1.
Characteristics of Veterans Health Administration (VHA) networks participating in Pain Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO).

IQR = interquartile range, No. = number.

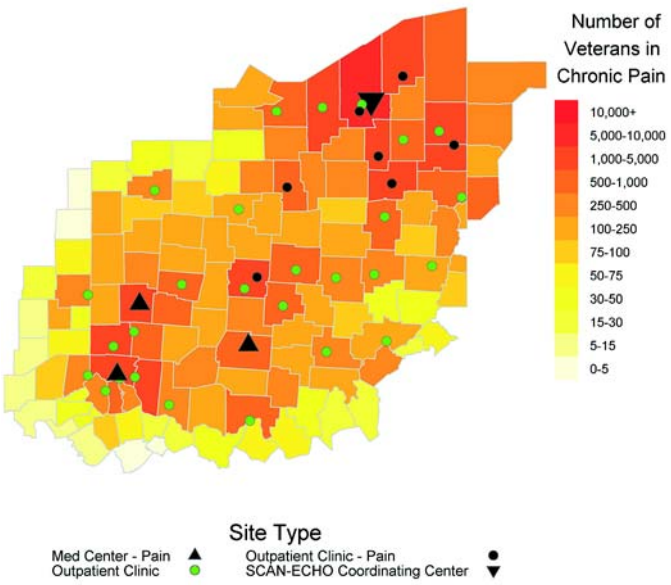

Figure 2.
Geographic distribution of Veterans with chronic pain in sample health network, including Veterans Health Administration medical centers (Med Center) and clinics both with and without pain specialty care available. SCAN-ECHO = Specialty Care Access Network-Extension for Community Healthcare Outcomes.

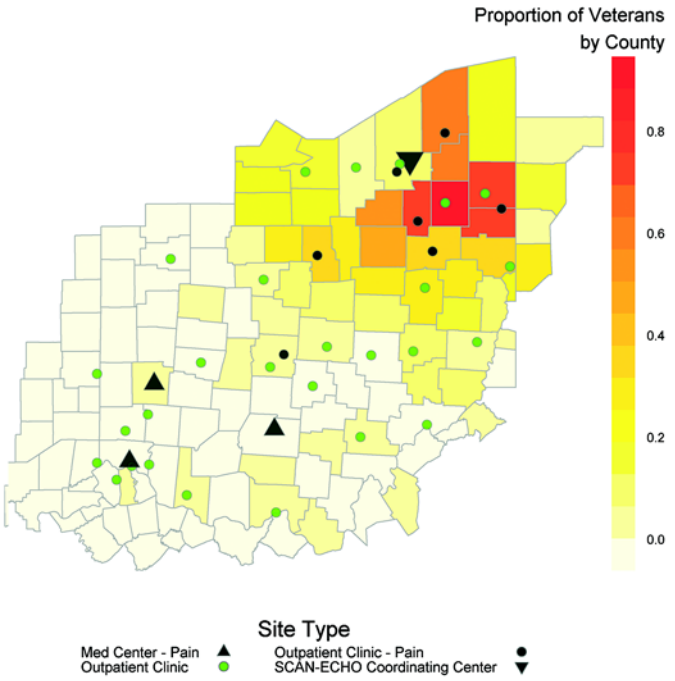

Figure 3.
Geographic distribution of probability of SCAN-ECHO exposure by county for Veterans with chronic pain in sample health network, including Veterans Health Administration medical centers (Med Center) and clinics both with and without pain specialty care. SCAN-ECHO = Specialty Care Access Network-Extension for Community Healthcare Outcomes.

Veterans living in urban areas around a medical center (**Figure 2**). Within this network, Veterans living in counties furthest from the coordinating SCAN-ECHO site had a lower probability of access to a provider participating in the Pain SCAN-ECHO program (**Figure 3**). Conversely, Veterans living closer to the coordinating SCAN-ECHO site were more likely to be treated by a provider who had presented a SCAN-ECHO session. Thus, rural Veterans living further away from the SCAN-ECHO coordinating center had a lower probability of being affected by Pain SCAN-ECHO than rural Veterans living closer to the coordinating center. Veterans living further from specialty pain care sites appeared to be less likely to be seen in-person at a specialty pain clinic (**Figure 4**).

Association Between Distance and Outcomes

Across all regions, increasing distance to specialty pain care was associated with significantly lower odds of being seen in-person in a specialty pain clinic (**Table 2**). For every 50-mile increase in Veteran distance from home to specialty pain care, there was a 22 percent lower odds of being seen in person at a specialty pain care clinic (OR = 0.78 per 50-mile increase, 95% CI = 0.77–0.79, $p < 0.001$). In contrast, for every 50-mile increase in Veteran distance from home to pain specialty care, there was only a 2 percent lower odds of access to a Pain SCAN-ECHO participating primary care provider (OR = 0.98 per 50-mile increase, 95% CI = 0.97–0.99, $p = 0.01$). Logistic regression models stratified by healthcare network revealed large heterogeneity in these results (**Table 2**). Two of seven regions showed a positive association between distance and Pain SCAN-ECHO pro-

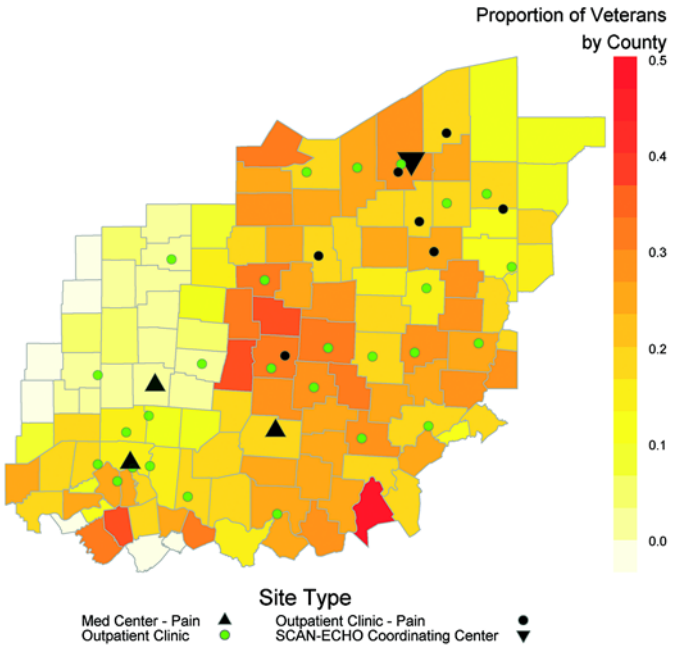

Figure 4.
Geographic distribution of probability of receiving in-person pain specialty care by county for Veterans with chronic pain in sample health network, including Veterans Health Administration medical centers (Med Center) and clinics both with and without pain specialty care. SCAN-ECHO = Specialty Care Access Network-Extension for Community Healthcare Outcomes.

vider participation, indicating Veterans with greater distance to the neare st specialty pain care site had a higher probability of access to a Pain SCAN-ECHO participating provider. Conversely, five of seven regions had a negative association, indicating Veterans living closer to the nearest specialty pain care site had a higher probability of access to a Pain SCAN-ECHO participating provider.

Table 2.
Table of logistic regression model results; odds ratios and 95 percent confidence intervals per 50-mile increase in distance.

Health Network	Seen In-Person at Pain Clinic	Touched by Pain SCAN-ECHO
All	0.78 (0.77–0.79)	0.98 (0.97–1.00)
1	0.96 (0.92–1.00)	0.81 (0.75–0.86)
2	1.07 (1.00–1.11)	0.76 (0.63–0.91)
3	0.94 (0.90–0.98)	0.80 (0.73–0.88)
4	0.84 (0.78–0.90)	0.15 (0.13–0.16)
5	0.76 (0.74–0.77)	1.67 (1.62–1.71)
6	0.77 (0.75–0.78)	0.61 (0.59–0.64)
7	1.07 (1.04–1.11)	6.25 (5.98–6.52)

Note: Two outcomes were used: Pain Clinic and Pain SCAN-ECHO provider participation. Separate models were fit for all networks. Primary predictor is distance from Veteran home to nearest in-person pain specialty care, with odds ratio presented per 50 mile increase.
SCAN-ECHO = Specialty Care Access Network-Extension for Community Healthcare Outcomes (SCAN-ECHO).

DISCUSSION

The objective of this study was to evaluate the spatial reach of the VHA 's Pain SCAN-ECHO program. We investigated spatial reach, or Veterans' access to a participating primary care provider, in two distinct ways. First, GIS mapping indicated that within a sample network, Pain SCAN-ECHO programs primarily touched Veterans closer to the SCAN-ECHO coordinating center. Rural Veterans living on the other side of the network were not touched by the program, but rural Veterans living closer to the coordinating center were touched. Second, using distance to the nearest in-person pain care as a surrogate for spatial access, we found the probability of Pain SCAN-ECHO provider participation was only mildly associated with distance to specialty pain care in the national cohort, suggesting that the Pain SCAN-ECHO program affected patients with both low and high spatial access to existing specialty pain care. Importantly, we found significant regional variation in these findings. Five of seven networks showed a negative association, indicating they disproportionately affected those patients with better spatial access. The remaining two networks showed a strong positive relationship, indicating Pain SCAN-ECHO disproportionately affected patients with low access to specialty pain care, consistent with the goals of the program. This evaluation is the first study to assess the geographic reach of a technology-based healthcare program in the context of the relevant underlying patient population, current healthcare system resources, and existing access to specialty care.

Prior studies of utilization as a function of spatial access have focused on in-person specialty care [15–19]. Our finding of decreased probability of in-person specialty pain care utilization as distance increases is consistent with those prior studies [15–19]. Among rural patients in North Carolina, increasing distance to care

was conversely associated with regular and chronic care utilization, although not acute care utilization [19]. A nationwide study of Veterans eligible for liver transplant showed increasing distance to a transplant center was associated with decreasing probability of receiving a liver transplant [18]. Rural Veterans have been shown to have decreased access to hepatitis C specialty care than their urban counterparts [20]. Our findings add to this list by exploring access to technology-based specialty care in addition to in-person specialty care.

GIS techniques have been previously used in evaluation of telemedicine programs. Maps of Project ECHO coordinating sites and mentee sites in New Mexico showed large spatial penetration of mentee sites in New Mexico across different specialty care areas [21]. A nationwide GIS analysis of VHA SCAN-ECHO across all specialties visualized coverage of mentee sites [6]. A regional U.S. telehealth program was evaluated using GIS and demonstrated substantial travel savings associated with telehealth visits compared with hypothetical in-person visits [8].

Several prior studies of Project ECHO programs have examined barriers to implementation of Project ECHO-type programs at the provider and program level [2,22–23]. Providers participating in a Project ECHO program identified the lack of protected time as a main barrier to participation, given their competing clinical duties in high-volume clinics [2,22]. Providers also identified a lack of administrative support as a barrier to participation [2]. Another study noted the main threat to the continuation of their Project ECHO program was financial [23]; the program is funded by grants, but administrative support or reimbursement programs that incentivize these programs are required for the longevity of the programs. These studies all highlight potential reasons why the observed uptake of Pain SCAN-ECHO was variable by region.

Our study has several advantages compared with the existing literature. We included the entire target population (Veterans with chronic pain) of the Pain SCAN-ECHO program. By calculating the distance to in-person specialty pain care resources for all Veterans with chronic pain in a network, we were able to contextualize the spatial penetration of the Pain SCAN-ECHO program against existing in-person specialty pain care utilization. No prior study has used maps to simultaneously visualize the full target patient population, system resource locations, probability of utilization of existing specialty care, and probability of primary care provider participation in the telementoring project. Finally, using patient data from the largest integrated medical system in the United States across seven geographically diverse regions with distinct Pain SCAN ECHO programs, we were able to characterize heterogeneity in implementation across sites.

There are two related but distinct findings that should inform future VHA policy. First, GIS mapping of SCAN-ECHO participation can identify geographic trends with respect to the coordinating site and provide novel insights into program uptake. Our maps suggest that within most participating networks, the Pain SCAN-ECHO programs primarily affected providers and patients who live in relatively close proximity to the coordinating SCAN-ECHO center. In this pilot program, funding mechanisms focused on the coordinating center. A combination of funding and existing intra professional relationships are the likely explanations for this finding. Clinics at further distances from the coordinating center may have less administrative support for the program as a result of decreased intraprofessional leadership contact, leading to lower provider participation rates. Future SCAN-ECHO expansion should seek to understand barriers to provider engagement and should specifically target provider engagement in clinics independent of distance to SCAN-ECHO coordinating sites. Administrative support for these programs will be key.

Second, the distribution of Pain SCAN-ECHO provider participation varied widely across the seven participating networks. Overall, we found that SCAN-ECHO provider participation was not associated with distance to specialty pain care, while in-person pain care was negatively associated with distance. However, examining these trends by network showed clear heterogeneity across networks with Pain SCAN-ECHO provider participation positively associated with distance to existing specialty pain care in some networks and negatively associated in others. This heterogeneity may be explained by a combination of variable local implementation strategies and intraprofessional networks as well as variable baseline traits of networks. Prior work has identified administrative support and protected time for participants as a main barrier to participation. Administrative support is likely variable by center (and therefore region), which may contribute to our observed heterogeneity. The distribution of distance to the nearest specialty pain care resources varied considerably by network, which is likely a function of both overall population density and the dis-

tribution of existing specialty pain care resources in a given network. Given the observed network heterogeneity, evaluation of Pain SCAN-ECHO and other regionally implemented programs should be completed at the network level to guide future implementation.

This analysis provides a framework for targeting the future spread of Pain SCAN-ECHO programs in the VHA as well as other technology-based programs. First, the analytic techniques employed are generalizable beyond the focus of Veterans with chronic pain. GIS techniques hold the potential to identify clusters of patients with low access to in-person specialty care resources and high incidence of disease regardless of disease process. Evaluation of existing technology-based healthcare programs and guidance of future expansion should consider the spatial distribution of the target patient population, the location of existing healthcare system resources, and the location of proposed new healthcare resources. If a primary goal of the program is to extend specialty care access to patients who are currently underserved, an understanding of the current location of patients and resources is critical to finding high-value targets for expansion of resources. Second, the finding of significant network variation is also informative outside of the VHA. Integrated healthcare systems that cover large and variable geographic areas will almost certainly have regional variation in specialty care availability as well as heterogeneity in implementation of programs in these regions. Region-specific GIS analysis as described here can guide administrators in allocating new specialty care resources.

Interpretation of this study requires recognizing potential limitations. First, any cohort study of administrative data may suffer from confounding due to unmeasured variables. Second, all distance calculations used geodesic ("as the crow flies") distance, which underestimates driving distance. However, prior work has shown a high correlation between geodesic and travel distance [24], especially at higher miles. The primary aim of this study was to contrast distance associations between models and networks, so this potential underestimation should cancel out across comparisons. Third, patient-level Pain SCAN-ECHO reach was defined based on linking presented patients to their primary care providers. Providers who attended Pain SCAN-ECHO sessions but did not ever present patients were not captured as participating providers, thus we may be undercounting exposed patients. Finally, in-person specialty pain care sites were defined based on the frequency of outpatient pain clinic records. This binary classification represents a nonbinary underlying spectrum of pain care services. It is possible that sites with a small number of pain visits have been misclassified as nonpain care sites. However, only a small percent of sites were on the threshold, and a sample of 15 of these threshold sites that were contacted directly all offered some form of specialty pain care.

CONCLUSIONS

Among Veterans with chronic pain receiving care in VHA settings, the association between distance to in-person pain specialty care and Pain SCAN-ECHO provider participation was highly variable by region. GIS-based analyses of patient and system resource locations can improve our understanding of program implementation and should inform outreach strategies for technology-based healthcare programs to strategically target Veterans with low access to care.

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Author Contributions:

Study concept and design: E. P. Carey, J. W. Frank, R. D. Kerns, P. M. Ho, S. R. Kirsh.

Data collection: E. P. Carey.

Data analysis: E. P. Carey.

Data interpretation: E. P. Carey, J. W. Frank, R. D. Kerns, P. M. Ho, S. R. Kirsh.

Drafting of manuscript: E. P. Carey, J. W. Frank.

Critical revision of manuscript for important intellectual content: E. P. Carey, J. W. Frank, R. D. Kerns, P. M. Ho, S. R. Kirsh.

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Participant Follow-Up: The authors have no plans to notify the study subjects of the publication of this article because of a lack of contact information.

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Appendix

Survey Questions

The purpose of this survey is to gather information on how researchers have used VA electronic and administrative data to identify pain. Your answers and comments will provide guidance for pain researchers.

Instructions:

1. This survey is anonymous; please do not include any personally identifying information.
2. We are asking about your (or your teams) use of VHA electronic and administrative data ***only***.
3. Please attempt to answer all items

1. What is your *primary* affiliation? (Choose 1 that best applies)

[] VHA

[] DOD

[] University

[] Other

If **Not** VHA, do you have VA WOC status? [] Yes [] No

2. What is your professional discipline? (Check all that apply)

() Chiropractic (DC, DCM)

() Doctoral level nurse (PhD, DNSc, DNP)

() Economist (PhD)

() Epidemiologist (PhD, DrPH)

() Pharmacist (PharmD, RPh)

() Physician (MD, DO)

() Physician Assistant (PA)

() Physiotherapist (DPT)

() Psychologist (PhD, PsyD)

() Statistician/Biostatistician (PhD)

() Social Worker

() Other, please specify: _______

3. What is your primary service or department? (Choose 1 that best applies)

[] General Medicine/Internal Medicine

[] Neurology

[] Nursing

[] Mental Health/Psychiatry

[] Pharmacy

[] Research

[] Women's Clinic

[] VACO

[] Other, please specify: _____

4. What is the primary focus of your pain research? (Choose 1 that best applies)

[] Back Pain

[] Blast-Related Injuries, including TBI

[] Cancer

[] Chronic Pain

[] Headache

[] Musculoskeletal

[] Neuropathic pain

[] Pain treatment

[] Palliative Care

[] Spinal Cord Injury

[] Surgical or peri-operative pain

[] Other, please specify: _____

5. In what VHA care settings have you conducted pain research? (Check all that apply)

() Inpatient

() Outpatient

() Emergency Department

() Surgical

() Other, please specify: _____

6. Have you been PI or co-PI on any funded research where pain is the *primary* focus?

[] No

[] Yes

6a. If YES, what was the source of funding for your most *recent* pain-related research?

[] VHA

[] DOD

[] NIH

[] Other

7. Have you used any of these VHA electronic and administrative data in research to identify the presence of pain? (Check all that apply)

		How valid do you think this data is, even if you have NOT used it?
	Used to identify the presence of pain?	**1 not valid – 7 valid**
CPRS notes	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
CPT codes	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
Chief complaint	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
Discharge summary	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
ICD9 codes	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
Pain NRS scores	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
Pharmacy	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
Stop codes	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦
Other: _____	() No () Yes	① ② ③ ④ ⑤ ⑥ ⑦

8. Have you used any of these other VHA resources in your pain research? (Check all that apply)

() Beneficiary Identification & Records Locator System (BIRLS) - Death File

() Corporate Data Warehouse (CDW)

() Decision Support System (DSS)

() Bar Code Medication Administration (BCMA)

() Health Analysis and Information Group (HAIG) Pain Management Survey data

() Health Economics Resource Center (HERC)

() Medical SAS Datasets (a.k.a. Austin data)

() National Surgical Quality Improvement Program (NSQIP)

() Northeast Program Evaluation Center (NEPEC)

() Serious Mental Illness Treatment Resource and Evaluation Center (SMITREC)

() Survey of Healthcare Experiences of Patients (SHEP)

() VA Information Resource Center (VIReC)

() Other VHA data source(s) _____

() I have not used any VHA electronic or administrative data sources or resources for pain research **(GOTO BARRIERS)**

The next questions ask about your most <u>recent</u> research using VHA electronic and administrative data:

9a. how did you define pain (e.g. back pain was defined using ICD codes 724, 7240x, 7241x, 7242x, 7243x, 7244x, 7245x, 7246x, 7247x, 8460x, or 8472x; a pain NRS score of 4 or greater; etc.)

9b. did you distinguish between chronic and acute pain?

[] No

[] Yes

9b1. If YES, how did you define chronic pain (e.g. 2 or more NRS of 4 or greater in a one year period)?

9c. did you construct a comparison or control group (e.g. pts. without pain)?

[] No

[] Yes

9d. did you examine recurrence of pain?

[] No

[] Yes

9e. what geographic area did you examine?

[] Single clinic

[] Local VA facility

[] VISN

[] Region

[] National

[] Other

10. Have you published any pain-focused peer-reviewed papers using VHA electronic and administrative data?

[] No

[] Yes

11. Are following barriers to your use of VHA electronic and administrative data for pain-related research? (Check all that apply)

	(1) Not a Barrier	(2) Minor Barrier	(3) Major Barrier
Concerns about data quality (e.g. completeness, lack of validation)	□	□	□
Concerns about data security	□	□	□
Data management issues (cleaning data, etc.)	□	□	□
Inability to access the data	□	□	□
Insufficient level of detail in the data	□	□	□
Lack of expertise in analyzing the data	□	□	□
Lack of hardware to house the data (computer storage)	□	□	□
Lack of standardization of data (e.g. site variation)	□	□	□
Privacy/HIPAA concerns	□	□	□
Timeliness of data	□	□	□
None of the above	□	□	□
Other	□	□	□

_____			

12. Do you think VHA electronic and administrative data are adequate for pain research?

[] No

[] Yes

13. How would you improve VHA electronic and administrative data for pain research?

14. Would you be willing to participate in an expert panel to discuss issues in pain research using VHA data?

[] No

[] Yes

15. Other Comments: (optional)

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Appendix 1. Pain-related medications that were included in present study.

Exposure Definition	Drug Class	Drug Name
Opioids	Opioids	Hydrocodone
		Oxycodone
		Morphine
		Methadone
		Fentanyl
		Meperidine
		Hydromorphone
		Oxymorphone
		Codeine
		Tramadol
Nonopioids		Acetaminophen
	NSAIDs	Aspirin
		Indomethacin
		Naproxen
		Ibuprofen
		Celecoxib
	SSRIs	Citalopram
		Paroxetine
		Sertraline
		Fluoxetine
		Escitalopram
		Fluvoxamine
	SNRIs	Duloxetine
		Venlafaxine
		Desvenlafaxine
		Milnacipran

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Appendix 2. Associations of combined primary care and mental health and/or rheumatology utilization and pain-related medication prescriptions (opioid or nonopioid), 12 mo following index fibromyalgia diagnosis date among **male** (*n* = 4,441) and **female** Veterans (*n* = 1,526).

Model Variable	<4 PC Visits Only	≥4 PC Visits Only	≥4 PC Visits & MH	≥4 PC Visits & RH	≥4 PC Visits, MH & RH
≥2 Opioid Prescriptions					
Relative Risk (95% CI)					
Males, Model 3*	1.00 (reference)	2.02 (0.88-4.63)	2.25 (1.15-4.42)	1.02 (0.16-6.51)	2.32 (1.16-4.67)
Males, Model 4†	1.00 (reference)	1.43 (0.73-2.80)	1.83 (1.09-3.08)	1.00 (0.27-3.69)	1.89 (1.11-3.20)
Males, Model 2	0.50 (0.22-1.23)	1.00 (reference)	1.09 (0.65-1.84)	0.52 (0.09-3.06)	1.10 (0.64-1.89)
Females, Model 3*	1.00 (reference)	2.53 (0.31-20.97)	2.96 (0.46-19.05)	**	3.00 (0.45-19.95)
Females, Model 4†	1.00 (reference)	2.61 (0.28-24.10)	4.25 (0.65-27.68)	**	4.15 (0.63-27.27)
Females, Model 2	0.47 (0.05-4.13)	1.00 (reference)	1.39 (0.42-4.60)	**	1.32 (0.39-4.43)
≥2 Nonopioid Prescriptions					
Relative Risk (95% CI)					
Males, Model 3*	1.00 (reference)	3.38 (0.99-11.59)	7.11 (2.40-21.06)	2.00 (0.27-14.80)	8.00 (2.65-23.52)
Males, Model 4†	1.00 (reference)	2.66 (1.17-6.04)	4.76 (2.35-9.64)	2.57 (0.78-8.48)	5.18 (2.55-10.51)
Males, Model 2	0.29 (0.08-1.02)	1.00 (reference)	2.05 (1.13-3.70	0.59 (0.10-3.53)	2.28 (1.25-4.14)
Females, Model 3*	1.00 (reference)	1.05 (0.26-4.24)	2.24 (0.83-6.03)	0.94 (0.22-4.03)	2.44 (0.90-6.57)
Females, Model 4†	1.00 (reference)	1.67 (0.45-6.19)	3.27 (1.17-9.10)	1.88 (0.49-7.22)	3.49 (1.25-9.74)
Females, Model 2	0.97 (0.24-3.90)	1.00 (reference)	2.13 (0.79-5.76)	0.83 (0.20-3.38)	2.26 (0.83-6.10)

*Model 3 adjusts for same variables in Model 2 in addition to year of index fibromyalgia diagnosis (10 nonreferent indicator variables for calendar years 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011) and whether index fibromyalgia diagnosis was in rheumatology setting.

†Model 4 is same as Model 1, excluding individuals with 1 diagnosis of anxiety, posttraumatic stress disorder or depression.

**Too few events limited risk estimation.

CI = confidence interval, PC = primary care, MH = mental health, RH = rheumatology, Rx = prescription.

Krein SL, Bohnert A, Kim HM, Harris ME, Richardson CR. Opioid use and walking among patients with chronic low back pain.
J Rehabil Res Dev. 2016;53(1):107–16.
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APPENDIX

	Reported Opioid Use			No Reported Opioid Use		
	intervention (N = 44)	**usual care (N = 55)**	**P-value**	**intervention (N = 64)**	**usual care (N = 58)**	**P-value**
Morphine equivalent daily opioid dose category[a]						
Baseline	n = 44	n = 54		n = 63	n = 57	
0	9 (20)	8 (15)		58 (92)	54 (95)	
1-19	17 (39)	21 (39)	0.72	2 (3)	2 (3)	0.66
20-49	15 (34)	22 (41)		3 (5)	1 (2)	
≥ 50	3 (7)	3 (5)		0	0	
6 months	n = 43	n = 54		n = 60	n = 55	
0	19 (44)	21 (39)		52 (86)	44 (80)	
1-19	10 (23)	12 (22)	0.13	4 (7)	7 (13)	0.53
20-49	8 (19)	19 (35)		4 (7)	4 (7)	
≥ 50	6 (14)	2 (4)		0	0	
12 months	n = 43	n = 54		n = 59	n = 55	
0	22 (51)	26 (48)		49 (83)	45 (82)	
1-19	12 (28)	10 (19)	0.22	5 (8)	7 (13)	0.68
20-49	5 (12)	15 (28)		4 (7)	3 (5)	
≥ 50	4 (9)	3 (5)		1 (2)	0	

Cell values are n (%).

[a] In prior 6 months, based on the fill in the prior 100 days that is closest to the date of survey completion or the survey due date if not completed

Any opioid medications obtained outside the Department of Veterans Affairs healthcare system are not included

Becker WC, Fiellin DA, Black AC, Kostovich CT, Kerns RD, Fraenkel L. Initial development of patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy. J Rehabil Res Dev. 2016;53(1):xx–xx.
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Appendix 1. Expert panel item rating results, sorted by median response value within category.

Item*	**Median Response Value**	**Panelists rating a 1-3** n (%)	**Panelists rating a 4-6** n (%)	**Panelists rating a 7-9** n (%)
Harm-related items (47 raters)				
Have you felt sleepy or less alert when driving or operating machinery?	9	2 (4.3)	5 (10.6)	40 (85.1)
Have side effects of opiate medicine interfered with your work, family, or social responsibilities?	8	3 (6.4)	3 (6.4)	41 (87.2)
Have you had thoughts of hurting yourself?	8	4 (8.5)	4 (8.5)	39 (83.0)
Have you fallen?	8	2 (4.3)	9 (19.1)	36 (76.6)
Have you felt depressed?	8	4 (8.5)	7 (14.9)	36 (76.6)
Have you been bothered by side effects of opiate medicines?	8	3 (6.4)	9 (19.1)	35 (74.5)
Have you felt sedated?	8	6 (12.8)	6 (12.8)	35 (74.5)
Have you been in a car accident with you as the driver?	8	5 (10.6)	8 (17.0)	34 (72.3)
Have you been bothered by constipation?	7	2 (4.3)	9 (19.1)	36 (76.6)
Have you been bothered by feelings of dizziness?	7	4 (8.5)	14 (29.8)	29 (61.7)
Have you had trouble thinking clearly?	7	3 (6.4)	16 (34.0)	28 (59.6)
Have you had trouble concentrating?	7	5 (10.6)	14 (29.8)	28 (59.6)
Have you felt anxious?	7	5 (10.6)	15 (31.9)	27 (57.4)
Have you felt down?	7	9 (19.1)	11 (23.4)	27 (57.4)
Have you had trouble remembering?	7	3 (6.4)	19 (40.4)	25 (53.2)
Have you felt sluggish?	7	5 (10.6)	18 (38.3)	24 (51.1)
Have you lost interest in activities?	6	6 (12.8)	18 (38.3)	23 (48.9)
Have you been bothered by straining or squeezing to try to pass bowel movements?	6	7 (14.9)	17 (36.2)	23 (48.9)
Have you been bothered by hard stools?	6	6 (12.8)	19 (40.4)	22 (46.8)
Have you felt slowed down?	6	6 (12.8)	21 (44.7)	20 (42.6)
Have you been bothered by vomiting?	6	9 (19.1)	21 (44.7)	17 (36.2)
Have you been bothered by nausea?	6	7 (14.9)	24 (51.1)	16 (34.0)

Becker WC, Fiellin DA, Black AC, Kostovich CT, Kerns RD, Fraenkel L. Initial development of patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy. J Rehabil Res Dev. 2016;53(1):xx–xx.
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Have you been bothered by itchy skin?	6	10 (21.3)	23 (48.9)	14 (29.8)
Have you been bothered by sweating?	5	11 (23.4)	24 (51.1)	12 (25.5)
Efficacy-related items (46 raters)				
Have opiate medicines been helpful in relieving your pain?	8	3 (6.5)	5 (10.9)	38 (82.6)
Did pain interfere with your day to day activities?	8	4 (8.7)	5 (10.9)	37 (80.4)
Is the amount of pain relief you are obtaining from your current pain reliever(s) enough to make a real difference in your life?	8	5 (10.9)	6 (13.0)	35 (76.1)
Have you been disabled by pain (unable to work or participate fully in activities)?	8	6 (13)	7 (15.2)	33 (71.7)
Has your pain been adequately treated?	7	3 (6.5)	10 (21.7)	33 (71.7)
Did pain interfere with your enjoyment of life?	7	4 (8.7)	10 (21.7)	32 (69.6)
Did you feel emotionally tense because of pain?	7	4 (8.7)	16 (34.8)	26 (56.5)
Misuse-related items (46 raters)				
Did you use alcohol to help relieve some of the pain?	9	0 (0.0)	5 (10.9)	41 (89.1)
Were you given pain medications from more than one clinic?	9	1 (2.2)	4 (8.7)	41 (89.1)
Have you run out of pain medication early and had to call for refills?	9	2 (4.3)	3 (6.5)	41 (89.1)
Have you had to go to someone other than your prescribing physician to get sufficient pain relief from your medications (ie, another doctor, the Emergency Room)?	9	1 (2.2)	5 (10.9)	40 (87.0)
Have you had to buy pain medications on the street?	9	2 (4.3)	4 (8.7)	40 (87.0)
Have you taken your medications differently from how they are prescribed?**	9	1 (2.2)	6 (13.0)	39 (84.8)
Have you needed to take pain medications belonging to someone else?	9	2 (4.3)	5 (10.9)	39 (84.8)
Have you gone to other physicians including emergency room doctors, seeking more of your pain medication?	9	2 (4.3)	5 (10.9)	39 (84.8)
Have you felt that you could not control how much or how often you used opiate medicine?	9	2 (4.3)	7 (15.2)	37 (80.4)
Have you needed to take pain medication more often than it is prescribed in order to relieve your pain?	9	3 (6.5)	6 (13.0)	37 (80.4)
Have family members or friends obtained pain medications for you?	8	2 (4.3)	7 (15.2)	37 (80.4)
Have you used the pain medications to help other symptoms such as problems sleeping?	8	2 (4.3)	7 (15.2)	37 (80.4)

Becker WC, Fiellin DA, Black AC, Kostovich CT, Kerns RD, Fraenkel L. Initial development of patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy. J Rehabil Res Dev. 2016;53(1):xx–xx.
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Did you take your pain medication to relieve or cope with problems other than pain?	8	1 (2.2)	9 (19.6)	36 (78.3)
Have you wanted to stop using opiate pain medicines or to cut down on the amount of opiate medicines that you use?	8	1 (2.2)	9 (19.6)	36 (78.3)
Have you been worried that you might be dependent on or addicted to opiate pain medicines?	8	0 (0.0)	11 (23.9)	35 (76.1)
Have you used the pain medications to help other symptoms such as anxiety?	8	1 (2.2)	10 (21.7)	35 (76.1)
Have opiate medicines caused you to have problems with family, friends, or coworkers?	8	2 (4.3)	9 (19.6)	35 (76.1)
Have you been preoccupied with or thought constantly about use of opiate pain medicines?	8	3 (6.5)	8 (17.4)	35 (76.1)
Did you feel high or get a buzz after using your pain medication?	8	3 (6.5)	9 (19.6)	34 (73.9)
Have you lost your pain medications and needed them replaced?	8	3 (6.5)	9 (19.6)	34 (73.9)
Have others been worried about how you're handling your medications?	8	2 (4.3)	11 (23.9)	33 (71.7)
Have you had to visit the Emergency Room?	8	4 (8.7)	9 (19.6)	33 (71.7)
Have you used the pain medications to help other symptoms such as depression?	8	1 (2.2)	13 (28.3)	32 (69.6)
Are you worried about how you're handling your medications?	8	1 (2.2)	13 (28.3)	32 (69.6)
Have others complained that you are not doing things that need to be done, such as going to class, work, or appointments?**	8	3 (6.5)	11 (23.9)	32 (69.6)
Is anyone in your family or among your friends concerned that you might be addicted to pain medications?	7	3 (6.5)	9 (19.6)	34 (73.9)
Have you needed to use a higher dose of opiate pain medicine to get the same effect?	7	2 (4.3)	11 (23.9)	33 (71.7)
Have you had to increase the amount of pain medications you take?	7	3 (6.5)	11 (23.9)	32 (69.6)
Have you save up unused medications in case you might need them in the future?	7	1 (2.2)	14 (30.4)	31 (67.4)
Have you had trouble controlling your anger (eg, road rage, screaming, etc)?	7	2 (4.3)	15 (32.6)	29 (63)
Have you had to make an emergency phone call or show up at the clinic without an appointment?	7	3 (6.5)	14 (30.4)	29 (63.0)
Have you asked for an increase your prescribed dosage of pain medication in order to get relief?	7	4 (8.7)	13 (28.3)	29 (63.0)
Did you take your pain medication because you were upset?	7	1 (2.2)	18 (39.1)	27 (58.7)
Have you thought certain pain medications (such as Vicodin, codeine, or Percocet)	7	4 (8.7)	18 (39.1)	24 (52.2)

Becker WC, Fiellin DA, Black AC, Kostovich CT, Kerns RD, Fraenkel L. Initial development of patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy. J Rehabil Res Dev. 2016;53(1):xx–xx.
http://dx.doi.org/10.1682/JRRD.2014.11.0285

work better for you and you prefer to take them and not others?				
Do you believe you would feel better with a higher dosage of your pain medication?	6	5 (10.9)	17 (37)	24 (52.2)
Have you found it helpful to call your doctor or clinic to talk about how your pain medication is working?	6	5 (10.9)	17 (37)	24 (52.2)
Do you believe you are receiving enough medication to relieve your pain?	6	7 (15.2)	17 (37)	22 (47.8)
Have you been in an argument?	6	11 (23.9)	18 (39.1)	17 (37)

*highly-rated items shaded

**highly-rated item for which permission to use was denied

Becker WC, Fiellin DA, Black AC, Kostovich CT, Kerns RD, Fraenkel L. Initial development of patient-reported instrument assessing harm, efficacy, and misuse of long-term opioid therapy. J Rehabil Res Dev. 2016;53(1):xx–xx. http://dx.doi.org/10.1682/JRRD.2014.11.0285

Appendix 2. Preliminary version of the PRIOR

Opioid pain medications are medications like oxycodone, hydrocodone, morphine, fentanyl, hydromorphone, or methadone.

In the past 30 days…

1. Have you felt depressed?
2. Have you had thoughts of hurting yourself?
3. Have you felt overly drowsy?
4. Have you felt sleepy or less alert when driving or using machinery?
5. Have you been in a car accident with you as the driver?
6. Have you fallen?
7. Have you been bothered by side effects of opioid pain medications?
8. Have side effects of opioid pain medications interfered with your work, family or other responsibilities?

In the past 30 days …

1. Have opioid pain medications been helpful in relieving your pain?
2. Is the amount of pain relief you are obtaining from opioid pain medications enough to make a real difference in your life?
3. Did pain interfere significantly with your day-to-day activities?
4. Have you been disabled by pain (unable to work or participate fully in activities)?

In the past 30 days…

1. Have you needed to take opioid pain medications more often than prescribed in order to relieve your pain?
2. Have you run out of opioid pain medications early and had to call for refills?
3. Did you use more of your medication, that is, take a higher dosage, than is prescribed for you?
4. Have you lost your opioid pain medications and needed them replaced?
5. Have others been worried about how you're handling your opioid pain medications?
6. Are you worried about how you're handling your opioid pain medications?
7. Have opioid pain medications caused you to have problems with family, friends, or coworkers?
8. Did using opioid pain medications cause you to have serious problems either at home, work, or school?
9. Have you felt that you could not control how much or how often you used opioid pain medications?
10. Have you thought constantly about use of opioid pain medications?
11. Have you wanted to stop using opioid pain medication or cut down on the amount of opioid pain medications that you use?
12. Have you been worried that you might be dependent on or addicted to opioid pain medications?
13. Have you had to visit the Emergency Room?
14. Have you gone to other doctors including emergency room doctors, seeking more opioid pain medications?
15. Have you had to go to someone other than your prescribing doctor to get enough pain relief from opioid pain medications?
16. Were you given opioid pain medications from more than one clinic?
17. Have family members or friends obtained opioid pain medications for you?
18. Have you needed to take opioid pain medications that belong to someone else?
19. Have you had to buy opioid pain medications on the street?
20. Did you use alcohol to help relieve some of the pain?
21. Did you feel high or get a buzz after using your pain medication?
22. Have you used opioid pain medications to help other symptoms such as problems sleeping?
23. Have you used opioid pain medications to help other symptoms such as being nervous or anxious?
24. Have you used the pain medications to help other symptoms such as depression?
25. Did you take opioid pain medication to relieve or cope with problems other than pain?